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OPHTHALMOLOGY

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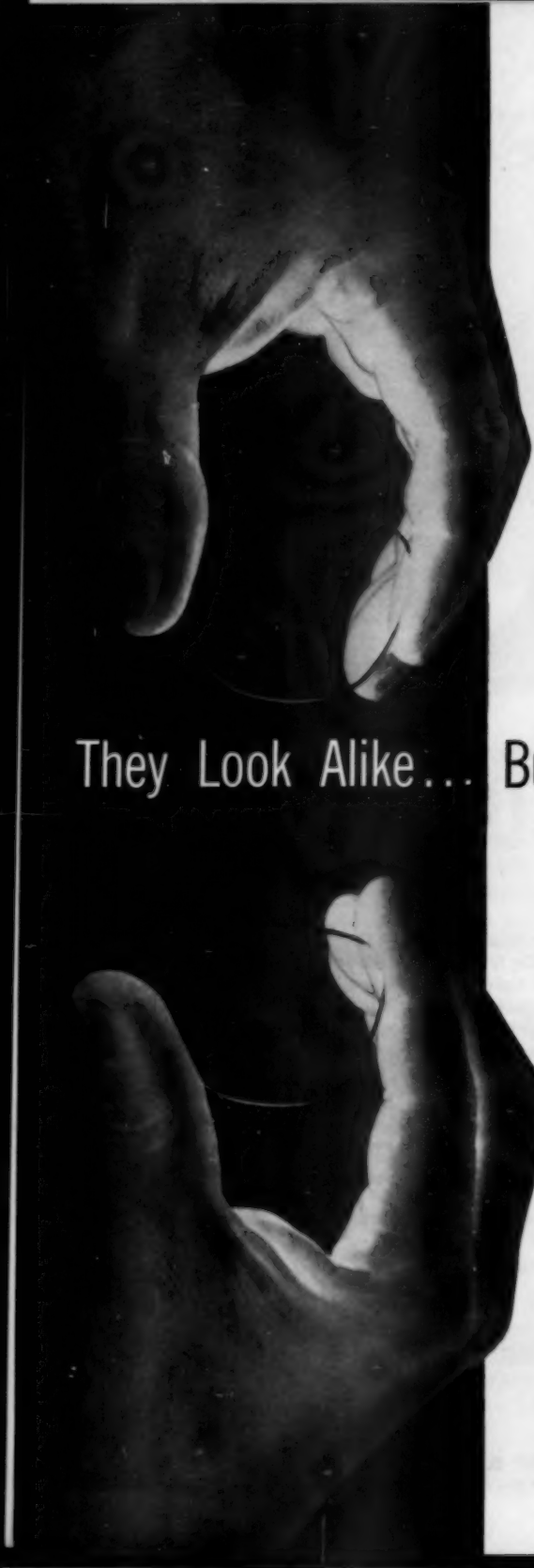

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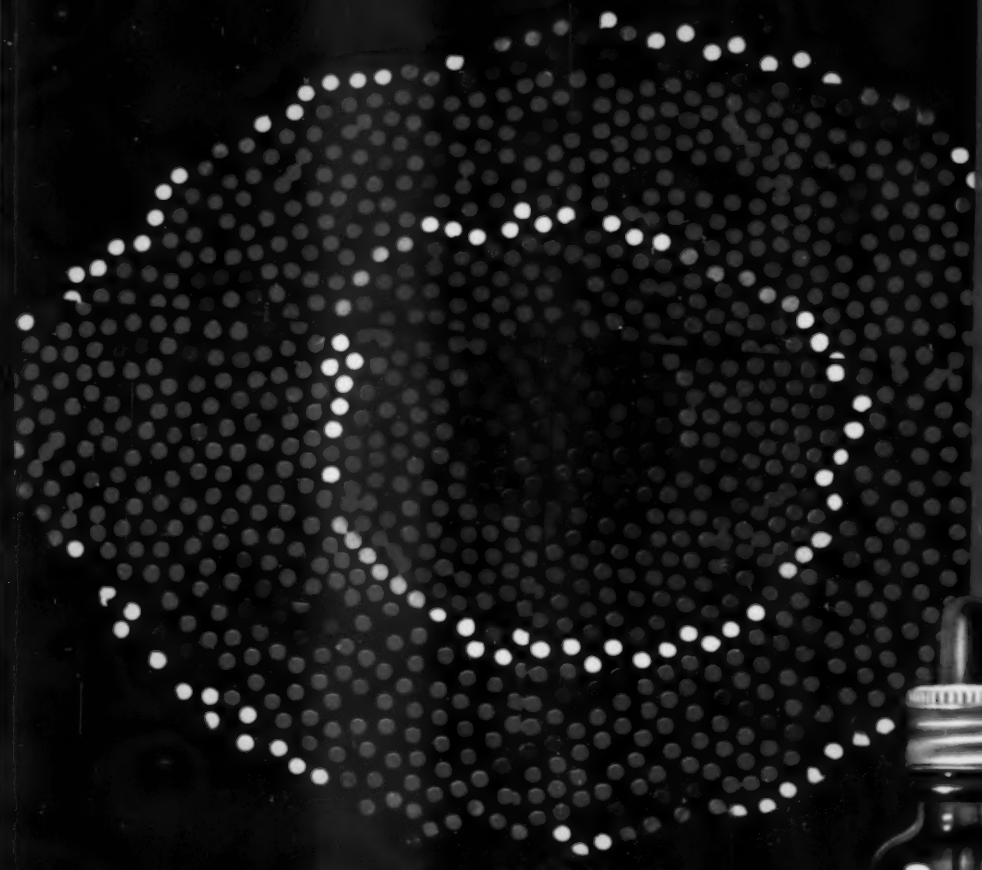

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1. Rosgorshek, R. H. and McIntire, W. C.: Am. J. Ophth. 40:34 (July) 1955. • 2. Ehrlich, L. H.: N. Y. State J. Med. 53:3015 (Dec. 15) 1953. • 3. Gettes, B. C.: A.M.A. Arch. Ophth. 51:467 (April) 1954. 4. Council on Pharmacy and Chemistry: J.A.M.A. 158:1523 (Aug. 27) 1955. • 5. Stoizer, I. H.: Am. J. Ophth. 36:110 (Jan.) 1953.

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1. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1287.
2. *Ibid.*, p. 1598.
3. *Am. J. Ophth.* 42:771, 1956.
4. *Am. J. Digest. Dis.* 22:5, 1955.
5. *Med. Times* 84:741, 1956.

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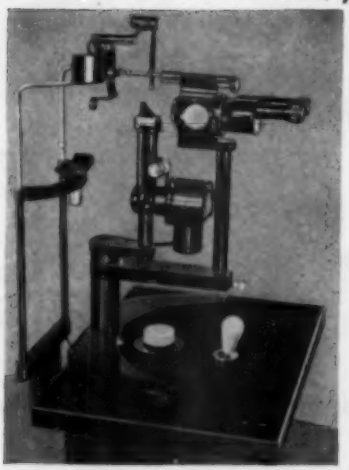

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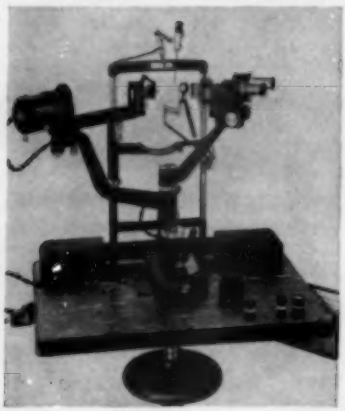

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Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education, and history 645

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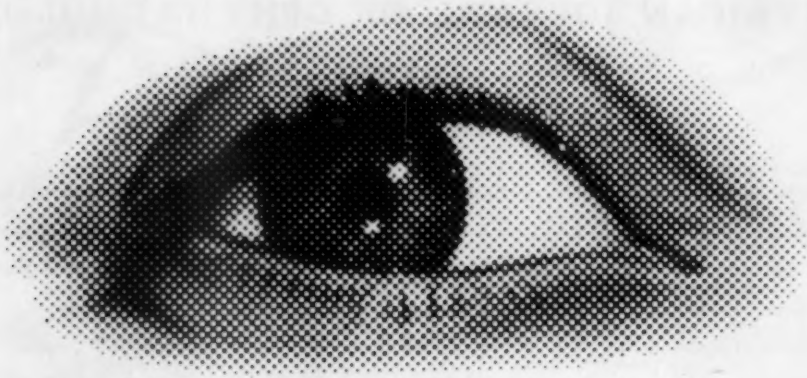

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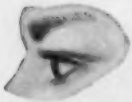

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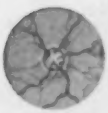

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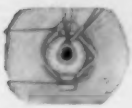

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THE FREQUENCY OF GLAUCOMA IN A SMALL URBAN COMMUNITY

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INTRODUCTION

There are, to our knowledge, no data on the prevalence of glaucoma in a community based on surveys of the total population. Estimates have been published for different countries,[1,2] but these either have been based on the limited experience in one hospital or ophthalmologic clinic in a large community or result from surveys, including tonometry, of selected or limited population groups.[3-8]

It seems desirable to know the prevalence and incidence of glaucoma in various populations. Such information might disclose differences in frequency in various geographic areas which could provide additional clues to etiology. Furthermore, the most accurate estimates obtainable are desired for the planning of glaucoma detection surveys and for planning for facilities and specialist's needs for care.

Ideally, a simple, safe, and accurate screening device is needed to locate glaucoma suspects, who can then be more thoroughly examined by standard ophthalmologic procedures. If such methods are applied to defined community or regional populations, all cases of early and advanced glaucoma could be located, and the desired frequency estimates of a clear description of the natural history of the disease might be obtained.

The development of such a screening device and such population surveys is still going on. In the meantime, as a result of tonometry surveys of several selected population groups, it has been stated that there are in the United States about 1,100,000 persons with unrecognized glaucoma.[9] Such estimates would seem to justify a greatly expanded program in glaucoma detection and treatment, preferably preceded by additional studies that might provide more accurate estimates of the extent of the problem. It will be necessary to determine carefully the validity of various screening and diagnostic procedures that may be used in such "early detection" programs.

A study that would provide statistics of improved accuracy for diagnosed glaucoma would seem worth while, and it is believed that this report is a step in that direction. We shall present statistics on the relative frequency of various forms of glaucoma and the prevalence in the total population of Rochester, Minnesota. We recognize that the prevalence statistics which are presented are the minimal rates for the existing glaucoma in this small community.

The medical facilities in Rochester, Minnesota, a community of 30,000 population, are to a large extent concentrated within the organization of the Mayo Clinic. Almost half

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the residents of the city are examined each year by Mayo Clinic physicians at the clinic, in one of the local hospitals, or at home for emergency house calls. The diagnoses made by each consultant during the patient's period of registry at the clinic are cross-indexed by means of a system using IBM punch cards and tabulating devices. It is a relatively simple task to obtain the records of all resident patients for practically any clinical disorder.

At the time of this study there were only a few physicians in general practice in the community. These physicians refer practically all patients with eye disorders of any serious nature to the large staff of ophthalmologists at the clinic. Routine ophthalmologic consultations are arranged for a high proportion of the medical patients who are examined in other sections of the clinic. A high proportion of all persons in the community are seen directly at the clinic for refraction or examinations for other ophthalmologic complaints. There are several optometrists in the community who handle routine refractions but who would be expected to refer to the clinic suspected cases of a serious medical or surgical nature.

We, therefore, assume that all residents of the community in whom glaucoma was suspected or diagnosed during the period of the study, 1945 to 1954, inclusive, were examined at the clinic. In some instances, glaucoma was diagnosed during an admission of the patient for complaints unrelated to vision; however, we did not determine the frequency with which glaucoma was diagnosed incidental to the patient's major complaint at the time of registration.

Method

The records of all patients who were residents of the city of Rochester, Minnesota, in whom the glaucoma had been diagnosed during the period 1945 to 1954, inclusive, were reviewed. Each case was then classified in keeping with our present terminology of glaucoma, and the patient's status was determined, as of the date for which prevalence was to be measured (December 31, 1954).*

Glaucoma is a complex of disorders in which abnormal intraocular pressure and its dire consequences are a common feature. The classification of the glaucomas adopted is as follows:

1. *Primary glaucoma.* Abnormal elevation of intraocular pressure is present without other recognized antecedent intraocular disease. This group is further subdivided:

a. Chronic simple glaucoma. Here the anterior chamber of the eye is of normal depth and configuration. Clinically, intraocular hypertension is noted and there is slowly progressive visual loss with few other symptoms.

b. Narrow-angle glaucoma. The anterior chamber angle is narrow or shallow and encroached on by peripheral anterior synechias. The so-called acute congestive glaucoma belongs to this group. Clinically, the disorder is characterized by episodic increases in intraocular pressure producing pain, congestion of the globe, and visual halos.

2. *Hydrophthalmos.* Glaucoma due to some congenital defects which interfere with the normal outflow of aqueous from the eye.

3. *Secondary glaucoma.* This is a complication of some other disease or damage to the eye. Here some etiologic factors such as uveitis, intraocular hemorrhage, dislocated lens, and so forth, are apparent, and intraocular pressure is sufficiently high to damage other ocular structures.

4. *Absolute glaucoma.* This diagnosis applies to those cases in which the eye is blind and the pressure is elevated.

Results

During the 10-year period covered in the study, 70 patients with glaucoma among the resident population of Rochester, Minnesota, were observed at the Mayo Clinic. Table 1 reveals that in two-thirds chronic

* The details of selection and the definition of resident population are described elsewhere.[20]

simple glaucoma was diagnosed. Secondary glaucoma accounted for 20 percent, and narrow-angle and absolute glaucoma accounted for seven and six percent, respectively. Table 2 also illustrates the number of patients whose onset of symptoms occurred and among whom the diagnosis was first made at the clinic during the period 1945 to 1954, inclusive, as well as the prevalence—that is, the number of patients living in the community on December 31, 1954.

Chronic simple glaucoma. There were almost three times as many cases of chronic simple glaucoma among females as among males, but correction for differences in the size of the population by sex reveals (table 3) that the prevalence rate for females is about twice that for males. In the older age

TABLE 1

TYPE OF GLAUCOMA AMONG RESIDENT POPULATION OF ROCHESTER, MINNESOTA, WHO WERE OBSERVED AT THE MAYO CLINIC, 1945–1954 INCLUSIVE

Type of Glaucoma	Male	Female	Both Sexes	Percentage of Total
Chronic simple	12	35	47	67
Narrow angle	0	5	5	7
Secondary	8	6	14	20
Absolute	2	2	4	6
Total	22	48	70	100

TABLE 2

GLAUCOMA AMONG RESIDENT POPULATION OF ROCHESTER, MINNESOTA, WHO WERE OBSERVED AT THE MAYO CLINIC, 1945–1954, INCLUSIVE, BY SEX

Type of Glaucoma	Male				Female			
	Total Number Observed*	Number with Onset in Rochester, 1945–1954	Number First Diagnosed during Residence in Rochester, 1945–1954	Prevalence: Residence in Rochester on 12/31/54	Total Number Observed*	Number with Onset in Rochester, 1945–1954	Number First Diagnosed during Residence in Rochester, 1945–1954	Prevalence: Residence in Rochester on 12/31/54
Chronic simple	12	7	8	7	35	17	22	19
Narrow angle	0				5	4	4	4
Secondary	8	7	7	7	6	5	5	3
Absolute	2	1	1	1	2	1	1	1
All types	22	15	16	15	48	27	32	27

* Includes those whose lnset occurred or whose first diagnosis was made prior to 1945 but who continued to be observed during the study period.

TABLE 3

GLAUCOMA: PREVALENCE AND PREVALENCE RATES FOR POPULATION OF ROCHESTER,* MINNESOTA, DECEMBER 31, 1954, BY SEX AND AGE

Age (yr.)	Population*		Chronic Simple Glaucoma				All Types of Glaucoma					
			Male		Female		Male		Female		Both sexes	
	Male	Female	No.	Rate/1,000 Population	No.	Rate/1,000 Population	No.	Rate/1,000 Population	No.	Rate/1,000 Population	No.	Rate/1,000 Population
0–24	4,937	6,454	0		0		2	0.4	0		2	0.2
25–44	4,000	4,899	0		0		3	0.8	0		3	0.3
45–54	1,560	2,056	0		1	0.5	0		1	0.5	1	0.3
55–64	1,338	1,625	6	4.5	3	1.8	6	4.5	4	2.5	10	3.4
65–74	781	1,125	1	1.3	6	5.3	3	3.8	9	8.0	12	6.3
75–84	330	519	0		6	11.6	0		9	17.3	9	10.6
85 plus	63	124	0		3	24.2	1	15.9	4	32.3	5	26.7
Total	13,009	16,802	7	0.5	19	1.1	15	1.2	27	1.6	42	1.4

* April, 1950, census.

groups, in which the chronic simple glaucoma prevalence rate is highest, females outnumber males almost two to one. Ordinarily, age-specific rates would provide the best comparison; the small number of cases in different age groups makes that difficult in the present study.

The age of onset for the seven male and 15 female patients in whom it was recorded averaged 68 years and was spread through the age period of 47 to 84 years. There was no significant difference in age at onset by sex.

The age distribution of patients living in the community on prevalence day is shown in Table 3. Among the females, there is the customary steady increase in the rate with age. The over-all rate is 0.5 per 1,000 for males and 1.1 per 1,000 for females. Among those residents 45 years of age and over, the rate is 1.7 per 1,000 for males and 3.5 per 1,000 for females.

Narrow-angle glaucoma. The diagnosis was recorded in five patients, all female. The ages at onset of symptoms ranged from 60 to 83 years (average 69 years). Four of the patients were still living in Rochester on prevalence day. Their ages at that time ranged from 65 to 84 years.

Hydrophthalmos. No cases were found.

Secondary glaucoma. This diagnosis was recorded in 14 patients. The glaucoma was associated with and presumably due to the following disorders: diabetic retinopathy, three; anterior uveitis, three; postoperative cataract complications, three; detached retina, one; contusion injuries to eye, three; retinitis proliferans, one. As might be expected, the ages varied considerably with the different causes and ranged from three years to 72 years at onset of symptoms. (In six of the 14, age at onset was less than 45 years.)

Absolute glaucoma. The diagnosis was made on four patients; two of these had died prior to prevalence day. Both surviving patients (one male, one female) were more than 85 years of age.

The age distribution on prevalence day for the surviving patients with *all* types of glaucoma is illustrated in Table 3. For the community as a whole the prevalence rate per 1,000 population is 1.2 for males, 1.6 for females, and 1.4 for both sexes combined. The rate for those 45-64 years of age is 1.7 per 1,000 population; the rate for those 65 years of age and over is 8.8 per 1,000 population.

Comment

We have presented a statistical analysis of diagnosed glaucoma in a specified population. It is recognized that the population is small and that chance fluctuation may well account for some of the oddities apparent in the distribution of cases by age or sex. However, the present study is believed worth reporting, because a very high proportion, if not all, of the population of a single community seeking medical and surgical ophthalmologic care are seen by the specialists at a single medical facility in which the records are carefully indexed by diagnosis. Furthermore, there appears to be a need to obtain prevalence statistical rates in such a fashion that they may be compared with the results of future studies.

The two items that might be considered here for discussion are, first, the relative proportion of different types of glaucoma as compared with those reported elsewhere and, secondly, the relative frequency of glaucoma in different populations. The first can be dismissed, because so many of the other analyses published utilize different systems of classification and because the patients observed at many of the hospitals or clinics are probably even less representative of all glaucoma cases in the community than in the present study.

In Figure 1 we have presented a comparison of the age-specific prevalence rates in Rochester, Minnesota (curve A), and that of some other recently reported surveys. The curve marked C is a combination of prevalence rates based on the studies by Brav and Kirber[4] in Philadelphia and by Koskenoja

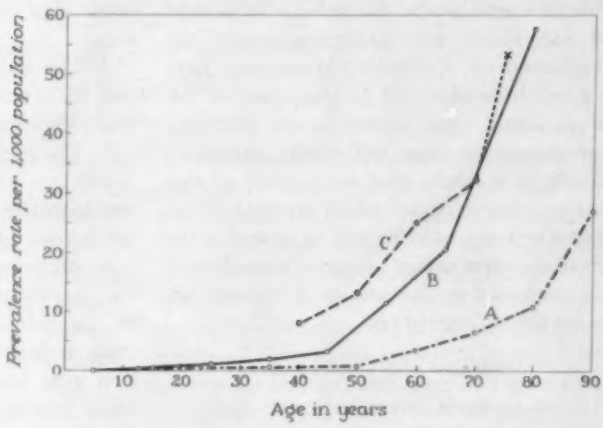

Fig. 1 (Kurland and Taub). Prevalence rates of glaucoma by age, based on tonometry surveys in Philadelphia and Helsinki (curve C), on ophthalmologic examinations of volunteers in three counties in Mississippi and Louisiana (curve B), and on glaucomatous patients resident in Rochester, Minnesota, on December 31, 1954 (curve A).

and Orma[7] in Helsinki, Finland. Brav and Kirber used tonometry as a screening technique among 10,000 industrial workers (mostly aged 45 to 65 years) in Philadelphia. Suspicious tonometry readings were followed by complete ophthalmologic examination. Of those examined, eight per 1,000 aged 40 to 65 years had advanced glaucoma and seven per 1,000 had early glaucoma. "Virtually none had any previous knowledge of their disease."[11] In a similar tonometry survey conducted among inmates of a home for the aged in Helsinki, Finland, and patients of the Helsinki Geriatric Outpatient Department, aged 65 years or more, 600 persons were examined. Glaucoma was diagnosed in 32 (5.3 percent) and in nine others the diagnosis was "borderline." Of the 32 with glaucoma, 28 had primary glaucoma and four had secondary glaucoma; and, of these, 15 with primary glaucoma and one with secondary glaucoma were first detected in the tonometry survey.

Curve B illustrates the prevalence rate by age for glaucoma based on ophthalmologic surveys of rural population in two counties in Mississippi and one parish in Louisiana. Routine tonometry was not employed; visual-acuity examinations followed by funduscopic examinations by an experienced ophthalmologist were carried out on about one third of the total population of the counties, who volunteered for the examinations. When glaucoma was suspected, visual fields, tonometry, and other tests were employed. The glaucoma prevalence rate was estimated as 2.6 per 1,000 of the total population of these counties. This is twice the over-all rate for Rochester, Minnesota. The number of individuals examined in the older age groups was relatively small but the steady rise of rates with age and the similarity of the results in this group with those of the preceding studies described in Philadelphia and Helsinki are striking, in spite of the different methods of compiling the samples of the populations which were examined.

The principal flaw in the comparison of the rates in Rochester with those of the other areas lies in the difference in the methods employed in collecting the data. It is unknown whether individuals with ocular symptoms in the eligible populations in the Philadelphia or in the Mississippi and Louisiana studies appeared more readily for examination than those without symptoms or whether the reverse may have happened, that is, that individuals who were relatively well and more mobile appeared for examination out of proportion to the total.

If the rates noted in the "tonometry surveys" are not based on biased samples and if there is no appreciable geographic differ-

ence, it would appear that at least 50 percent of individuals with glaucoma among the population of Rochester, Minnesota, have not yet been observed or diagnosed at the Mayo Clinic. Since chronic simple glaucoma has an insidious onset and usually progresses slowly, it is likely that early cases of this disease, that is, those which are said to respond best to treatment, will be missed to the greatest extent unless a routine examination for increased ocular tension is carried out in the elderly population.

Summary and Conclusions

1. A study is presented with statistics which illustrate the relative frequency of various forms of glaucoma and the prevalence of glaucoma which has been diagnosed in the total population of Rochester, Minnesota.

2. The data suggest that the prevalence rate of primary glaucoma is higher for females than for males.

3. The prevalence rate of glaucoma in the population is negligible below age 40 years but increases very rapidly with advancing age beyond age 40 years.

4. An attempt has been made to compare the prevalence rate of diagnosed glaucoma in the community with rates from other areas in which large groups of the population were first examined with tonometry or by a routine ophthalmologic examination. The age-specific rates obtained in those studies are appreciably higher than the rates noted in Rochester, Minnesota.

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GONIOTOMY FOR GLAUCOMA ASSOCIATED WITH NEVUS FLAMMEUS*

Successful operation in two cases

Otto Barkan, M.D.
San Francisco, California

Glaucoma is frequently associated with nevus flammeus (encephalo-oculocutaneous angiomatosis). In infancy and childhood it may develop the changes characteristic of congenital glaucoma or buphthalmos but it often does not attract attention for several years. In later years its course is similar to that of open-angle (chronic simple) glaucoma in the adult.

The treatment of glaucoma associated with nevus flammeus is, according to Duke-Elder, full of disappointments and frequently quite ineffectual. Some cases become arrested; a few respond to treatment; but absolute glaucoma with ultimate blindness is the usual end-result.[1]

Goniotomy under gonioscopic control[2-5] has proved successful in two eyes. In a third eye the pressure was only temporarily reduced by three goniotomies.

Case reports

Case 1

J. N., a 10-year-old girl, was first seen on September 14, 1950, with the complaint that the left eye had begun to turn out six months previously. She had been born with a port-wine nevus flammeus (fig. 1) involving the face (including all three branches of the fifth nerve), neck, and most of the surface of the rest of the body and extremities. The left eyeball had been larger at birth.

The general physical examination showed nothing abnormal except for the nevus. X-ray examination of the skull showed no abnormality. There were no mental defects, no history of epilepsy. The child has kept up well in school. Family history contributed nothing pertinent.

When first seen the tension in the right eye was 40 mm. Hg, in the left 60 mm. Hg (McLean) with miotics. There was an exotropia of the left eye of about 15 degrees. The vision was: R.E., 8/10 and J1: L.E., 1/10 correctible with a -1.75D. sph. $\bigcirc$ -0.25D. cyl. ax: 90° to 4/10 and J5. The corneal diameters in the horizontal meridian measured right 11.0 mm., left 12.75 mm. The scleras showed a bluish mottled appearance (nevus sclerae), the irises of both eyes were a very dark brown, and the fundus was extremely dark (melanosis bulbi).

Ophthalmoscopic examination showed a

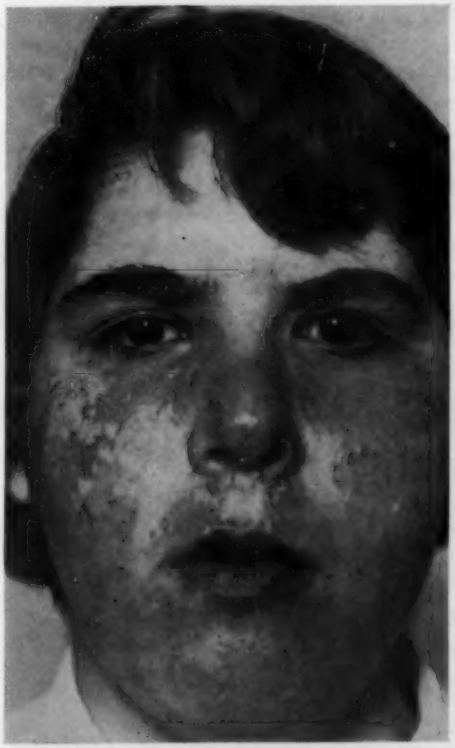

Fig. 1 (Otto Barkan). *Case 1.* Showing appearance of nevus flammeus.

* Read before the XVII International Congress of Ophthalmology, New York, September, 1954.

wide physiologic excavation on the right eye and on the left a glaucomatous excavation extending to a large part of the rim with some atrophy. The vessels of the right fundus appeared normal. The left fundus showed marked dilation and tortuosity of the veins.

Visual fields. The right eye was normal; the left showed a characteristic nasal contraction.

Gonioscopic examination. On the left eye the stroma of the very dark iris was reflected onto the angle wall. On the nasal side it covered the entire angle wall up to the line of Schwalbe; on the temporal side it covered the wall in varying degrees extending to the line of Schwalbe only in places. The portion which covered the angle wall was of a darker color. The stroma was devoid of crypts (fig. 2). On the right eye the changes were less extensive, the angle wall being exposed to aqueous to a much greater extent than in the left eye.

One drop of prostigmine (five percent) instilled every three hours failed to reduce the pressure more than a few millimeters.

Goniotomy with the glass was performed on October 3, 1950, on the left eye. Postoperative gonioscopy showed that the reflected stroma of the iris, which had covered the entire angle wall, was removed in three small areas. Three months later tension was: R.E., 60 mm. Hg; L.E., 48 mm. Hg (McLean), the last drops of miotic having been instilled 45 minutes previously. On January 9, 1951, goniotomy with the glass was repeated on the left eye. On March 20, 1951, tension in this eye was reduced to a normal of 31 mm. Hg. Gonioscopy showed four holes in the reflected iris through which the underlying angle wall could be seen.

Fig. 2 (Otto Barkan). *Case 1.* Showing removal of aberrant stromal tissue from angle wall.

Goniotomy with the glass was performed on the right eye on March 20, 1951. On April 23rd, the tension was: R.E., 32 mm. Hg; L.E., 32 mm. Hg (McLean), no drops having been instilled for three days. Gonioscopy of the right eye showed removal of the stromal tissue covering the angle wall between the 2- and 3-o'clock positions and a cleftlike separation of the angle wall in this region. On October 19, 1951, tension was: R.E., 48 mm. Hg; L.E., 36 mm. Hg, no drops having been instilled for three days.

A second goniotomy with the glass was performed on the right eye on an adjacent portion of the angle wall. Five months later, while tension in the right eye remained stationary, it was increasing in the left eye. On March 27, 1952, under general anesthesia tension was: R.E., 36 mm. Hg; L.E., 45 mm. Hg, with drops. Goniotomy on the left eye was done across the nose. On June 11, 1952, tension was: R.E., 36 mm. Hg; L.E., 44 mm. Hg, with miotics. A cyclodialysis on the left eye was performed.

On September 11, 1952, tension was: R.E., 55 mm. Hg; L.E., 34 mm. Hg, with miotics. Gonioscopy on the left eye showed a characteristic cyclodialysis cleft between the 1- and 2-o'clock positions. A goniotomy with the glass was performed on the right eye. During the operation a white wake appeared following the blade and a large clump of pigmented tissue collected on the end of the blade and dropped onto the anterior surface of the iris.

On April 23, 1953, the last goniotomy on the right eye having been performed seven months and a cyclodialysis on the left eye 10 months previously, tension was: R.E., 25 mm. Hg; L.E., 34 mm. Hg (McLean) no miotics having been instilled for 10 days.

On December 1, 1953 the tension was: R.E., 32 mm. Hg; L.E., 75 mm. Hg. A recurrence of increased tension in the left eye had occurred 16 months after the cyclodialysis. Gonioscopy showed the cyclodialysis cleft open at its entrance to the anterior chamber but external to this its bottom was closed. A cyclodiathermy was performed on the left eye.

On February 16, 1954, the tension of left eye was 46 mm. Hg without drops. A cyclodialysis was performed on the left eye. On February 24, 1954, the tension of the left eye was 50 mm. Hg and a cyclodiathermy was performed. On September 1, 1954, the last goniotomy on the right eye having been performed 20 months, and the cyclodiathermy on the left eye six months previously, tension was; R.E., 28 mm. Hg; L.E., 35 mm. Hg (McLean), no miotics having been instilled for 10 days. Vision was: R.E., 1.0; L.E., 0.2.

Gonioscopy on the right eye showed that the stromal tissue which had covered the angle wall had been removed from the 1- to 5-o'clock positions, exposing the angle wall to aqueous (fig. 2). The angle wall itself appeared untouched. The increased tension had evidently been the result of obstruction by aberrant stromal tissue.

In the left eye the tension, originally 50 mm. Hg, with miotics, was reduced by three incomplete goniotomies to tensions varying between 34 and 44 mm. Hg with miotics. In the stripped areas, which were not as extensive as in the right eye, the underlying angle wall (trabecula) appeared denser and more fibrous than normal which may have been the result of congenital thickening or of surgical trauma. It evidently accounted for the incomplete reduction of tension. It is interesting to note the excellent results of cyclodialysis in this eye for a period of 16 months at the end of which time a recurrence of tension occurred due to closure of the cleft. A second cyclodialysis and a cyclodiathermy were ineffective. A second cyclodiathermy has normalized the tension for a period of two months up to the present time.

Case 2

H. S. H., a six-year-old boy, was seen on September 17, 1951. He had been born with a hemangioma (oculocutaneous angiomatosis) involving eyelids, face, mouth, lips, and chin. It was very noticeable on the inner surface of the upper lip and on the upper gums running back over the palate. It was present also on the surface of the tongue. The upper jaw had become larger and more developed, probably as a result of the increased blood supply. At 17 months of age the eyes had clouded. A local ophthalmologist using general anesthesia found the pressure normal. However, the eyes were larger than average. Miotics were prescribed to be instilled every four hours.

The child was alert and except for the above-mentioned nevus was physically normal in every respect.

Ophthalmologic examination. The nevus flammeus which involved the skin of both lids did not appear to extend beyond the lid margins. The corneal diameters, measured in the horizontal meridians with an eye caliper, were 14.5 mm. bilaterally. The corneas were clear and the anterior chambers deep and equal. Vision on the kindergarten chart was 20/20 O.U.

Fundi. The right optic disc showed no cupping. The left disc showed only the suggestion of a physiologic cupping. There was no pallor. The retinal vessels showed a corkscrewlike tortuosity. In the left eye there was a vertical tear of Bruch's membrane (without history of trauma). In the adjoining area the fundus appeared slate gray.

Gonioscopic examination. The angle in both eyes presented the appearance of a low-grade congenital glaucoma. The iris was flat

and there was no sinus. The iris was inserted into a frontally placed surface presenting a shagreen and a rather marked circumferential weave with a few capillaries on its surface. On the right eye at the 7-o'clock position there was a limited area where the recess of the angle appeared normal. At other points the root of the iris was pulled up a little at its insertion. In the left eye all of these changes were more marked. The iris was inserted a little higher covering it at some points up to the line of Schwalbe but in other places leaving narrow clefts below the line.

Refraction estimated with the ophthalmoscope was: R.E., +2.0 D. sph.; L.E., +3.0D. sph. Tension was: R.E., 32 mm. Hg; L.E., 40 mm. Hg (McLean), no drops having been instilled for two days.

On September 18, 1951, goniotomy with the glass was performed on the left eye under intratracheal ether. On March 19, 1952, tension was: R.E., 29 mm. Hg; L.E., 38 mm. Hg. The area of stripping was very small. A goniotomy was performed on an adjoining sector. When last seen on June 15, 1953, 15 months postoperative, tension was: R.E., 36 mm. Hg; L.E., 34 mm. Hg (McLean), no miotic having been instilled for 10 days. The vision was: R.E., 6/10, correctible with a +0.37D. cyl. ax. 180° to 8/10; L.E., 0.5, correctible with a +0.5D. cyl. ax. 180° to 8/10.

In view of the history of cloudiness of the corneas at the age of 17 months, the gonioscopic findings, which were marked in the left eye, the enlarged corneas, the tear in the lamina vitrea, and the slightly higher tension in the left eye, it is suggested that this patient had a mild congenital glaucoma, associated with nevus flammeus with possibly a spontaneous arrest in the right eye. Goniotomy stripped a portion of the angle of the left eye and reduced the pressure from 40 to 32 mm. Hg, equaling the pressure of the right eye. This and the preoperative obstructive findings seen gonioscopically in the angle of the left eye suggest that the cause of the increased pressure was anomalous tissue associated with an anomalous insertion of the iris which partially obstructed the filtration angle.

Discussion

Three main theories have been presented to account for the increased intraocular pressure in glaucoma associated with nevus flammeus. Of these, the vascular theory (hemangioma of the choroid) is the most commonly accepted at the present time. Abnormality of sympathetic innervation (nervous theory) has been considered.

Developmental abnormality in the chamber angle (mechanical theory) has been supported by the anatomic examinations of Safar[6] and Salus.[7] They suggested that obstruction to outflow is caused by abnormal tissue in the chamber angle similar to that found in congenital glaucoma.

François[8] in 1951 emphasized that the mechanical theory is based only on supposition since the only two cases of glaucoma associated with nevus flammeus examined gonioscopically up to that time had shown a normal filtration angle.[9] From a review of the literature he concluded that the increased pressure has its origin in an angiomatosis of the choroid.

Anderson,[10] in 1939, reviewed 60 cases of hydrophthalmia with facial nevi, of which five included histologic examination. Of the latter, an angioma of the choroid was found in the majority, and all except one, which was an exceptional specimen, showed changes in the angle that are characteristic of congenital glaucoma. He believed the association of nevi with hydrophthalmia is probably coincidental, although the two conditions may result from a common cause, and that the main source of the hypertension is probably an anomalous state of Schlemm's canal and the adjacent meshwork.

In the two cases here presented (three eyes operated upon) postoperative gonioscopy showed a partial removal of the aberrant tissue which covered the angle wall.

There was no sign of incision of the angle wall, of external fistulization, or of communication with the suprachoroidal space to account for the reduction of pressure. The retention and glaucoma must have been due to obstruction of the angle by aberrant tissue, a conclusion which supports the mechanical theory of the cause of glaucoma associated with nevus flammeus. The angiomatosis which was present did not appear to have any causal relation to the increased pressure in these eyes.

Since goniotomy under gonioscopic control is without hazard, it is suggested that it is the operation of choice in cases of glaucoma associated with nevus flammeus in which gonioscopy shows an obstructive anomaly in the chamber angle. It produces no disfigurement. It preserves a round, central, freely reacting pupil. If the first procedure does not normalize the pressure it can be repeated in adjacent sections of the angle. Goniotomy does not interfere with the performance of a secondary operation which may be required. The need of early diagnosis and early operation is emphasized.

Summary

In three eyes afflicted with glaucoma associated with nevus flammeus gonioscopy showed the angle filled and the angle wall covered in varying degree by tissue which resembled iris stroma in appearance. There was an anterior insertion of the iris.

In two eyes goniotomy under gonioscopic control normalized the pressure and preserved vision for periods of three years and two years up to the present time. In a third eye the pressure was temporarily reduced by three goniotomies; two cyclodialyses and two cyclodiathermies have achieved normalization up to the present time.

Since goniotomy under gonioscopic control is without hazard it is suggested as the operation of choice in cases of glaucoma associated with nevus flammeus in which gonioscopy shows an obstructive anomaly in the chamber angle.

The theory of mechanical obstruction in the angle as the cause of glaucoma associated with nevus flammeus is supported by normalization of pressure by goniotomy in two cases (two eyes).

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THE EFFECT OF RAUWOLFIA SERPENTINA DERIVATIVES ON INTRAOCULAR PRESSURE*

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Although the stability of the level of intraocular pressure must be dependent to a considerable extent upon structural characteristics of the eyeball itself, the role of neural and/or humoral factors has also attracted attention.[1] It has been suggested that the hypothalamus is specifically concerned with the regulation of intraocular pressure. Indeed, direct stimulation of certain hypothalamic centers has been shown to alter ocular tension in animals.[2] Substances presumably of pituitary origin have been described which appear to influence the intraocular pressure.[3] It is conceivable that the effect of emotional stress on the course of glaucoma could be mediated through mechanisms of this sort.[4]

Preparations of Rauwolfia serpentina have recently been used extensively in the treatment of arterial hypertension, as well as in certain neuropsychiatric conditions. The action of the Rauwolfia alkaloids appears to depend upon an alteration of the interrelationships between the hypothalamus and other portions of the nervous system. The gross result of these effects suggests a relative diminution of sympathetic tonus and an increase in parasympathetic tonus. It has been postulated that the effect of the Rauwolfia alkaloids which have a sedative action (reserpine, deserpidine, and rescinnamine) is related in some manner to the release of serotonin (5-hydroxytryptamine) from nervous tissue and other depots.[5-8]

In view of the presumed locus of action and the nature of the pharmacologic effects of the Rauwolfia derivatives, and in keeping with the concept of the possible significance of neurohumoral factors in the regulation of intraocular pressure, an assessment of the effect of Rauwolfia on ocular tension was undertaken. The study was initiated in December, 1953, and consisted of two phases:

1. A long-term, double-blindfold evaluation of the influence of orally administered Rauwolfia preparations.
2. The determination of the effect of the intravenous administration of reserpine.

PART I: LONG-TERM ORAL ADMINISTRATION

METHODS

Patients were selected for participation in this study on the basis of two criteria. Individuals with glaucoma in one or both eyes were accepted if there was no reasonable anticipation that the particular therapeutic regimen under which they had already achieved maximum benefit would require alteration or embellishment by any of the standard medical or surgical procedures. The second criterion, which applied both to those with normal and with glaucomatous eyes, was based on the judgment of the investigators that the patient could be expected to follow instructions and to remain under observation for a prolonged period. As a result of these obligatory selection factors, the sample of patients included in this study cannot necessarily be taken as reflecting the characteristics of the population as a whole with regard to such parameters as age, sex, race, general medical condition, type, duration, and severity of glaucoma, or the presence of other diseases of the eye.

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A special weekly clinic was established for the purposes of this investigation. At each visit the patient was seen first by the ophthalmologist, who estimated the intraocular pressure in each eye with a Schiøtz tonometer. Discussion of progress, symptoms, and treatment was scrupulously avoided. The patient was then conducted to another room where the physician in control of the treatment estimated the blood pressure (sitting posture, right arm) and pulse, noted any symptoms which the patient might spontaneously mention, and prescribed further treatment.

At first the patients were observed during alternating periods of placebo and Rauwolfia therapy of six to eight weeks' duration. It soon became apparent, however, that somewhat longer periods of observation were advisable to allow any delay in onset and cessation of effect to become apparent. Such a lag effect has been well documented in the treatment of arterial hypertension with these drugs.[9] For this reason the alternating periods of placebo and active drug treatment were of 12 to 20 weeks' duration during the greater part of the investigation.

At no time did the individual who measured the intraocular pressure know whether any given patient was receiving placebo or genuine Rauwolfia medication. In order to minimize the effect of diurnal variation all examinations were conducted between 10:00 A.M. and 12:00 M. Conventional therapy was continued without change throughout the period of observation so that the Rauwolfia administration could be considered as the only therapeutic variable.

Since the Rauwolfia drugs may induce recognizable symptoms in some individuals, it is likely that the more observant patients would have little difficulty in detecting a change from placebo to active medication or vice versa. In order to minimize this factor, the number of tablets prescribed per day was always increased when treatment was changed from placebo to genuine Rauwolfia; and, contrariwise, whenever there was a transition from genuine to placebo medication the number of tablets was reduced. With this procedure the patients readily accepted the appearance or disappearance of symptoms as reflecting a change in dosage, without suspecting that sometimes they were taking placebos.

Three representative types of Rauwolfia serpentina preparations were utilized: tablets of the crude root, the alseroxylon fraction, and crystalline reserpine.* There was no attempt to compare their relative effectiveness.

The data from each eye were treated as an individual experiment, each eye serving as its own control. For the sake of simplicity it was elected to combine the observations during all of the placebo periods for comparison with the observations during all of the active drug periods, rather than to analyze individually each transition from placebo to drug or drug to placebo. Student's "t" test[10] was utilized to evaluate the difference between the mean of the estimations of tension during the placebo and the active drug periods. A probability value (P) of 0.05 or less was considered statistically significant.

Results

The eyes are divided into three groups, and the pertinent data are summarized in Tables 1, 2, and 3. Table 1 characterizes Group I which consists of 24 nonglaucomatous eyes in 15 patients. In spite of slightly elevated ocular pressure four eyes were classified with the nonglaucomatous group after prolonged observation failed to reveal substantiating evidence for a diagnosis of glaucoma (eyes numbered 19, 20, 21, and 22). The evaluations were based on from 19

*Tablets of crude root and placebos (Raudixin®) were supplied by The Squibb Institute for Medical Research; alseroxylon fraction tablets and placebos (Rauwiloid®) were furnished by Riker Laboratories, Inc.; and tablets of crystalline reserpine and placebos (Serpasil®) were provided by Ciba Pharmaceutical Products, Inc.

TABLE 1

GROUP I: NONGLAUCOMATOUS EYES, ORAL RAUWOLFIA

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
1	69 Cauc. F.	N	Wide	0	0	Als. 24 mg.	P50-G117-P87	20.1 ±2.62	21.2 ±2.10	22	1.128	>0.2	
2	69 Cauc. F.	N	Wide	0	0	Als. 24 mg.	P50-G117-P87	21.2 ±2.86	22.2 ±3.74	22	0.733	>0.4	
3	77 Cauc. F.	N	Wide	0	0	Als. 24 mg.	P50-G70-P21	18.3 ±2.18	18.1 ±3.07	17	0.189	>0.8	
4	77 Cauc. F.	N	Wide	0	0	Als. 24 mg.	P50-G70-P63	20.4 ±3.00	20.6 ±3.24	23	0.158	>0.8	
5	34 Cauc. F.	N	Wide	0	0	Als. 32 mg.	P51-G84-P63	19.5 ±1.97	20.0 ±1.65	26	0.712	>0.4	
6	34 Cauc. F.	N	Wide	0	0	Als. 32 mg.	P51-G84-P63	19.8 ±1.83	20.8 ±2.08	26	1.376	>0.1	
7	46 Cauc. F.	N	Narrow c̄ occ. goniosynechias	0	0	Als. 32 mg.	P100-G84-P77	18.7 ±3.10	17.8 ±2.83	32	0.904	>0.3	

Cauc., Caucasian
F., Female
M., Male
N, no evidence of glaucoma

Pilo., Pilocarpine nitrate
Als., Alseroxylon fraction
Res., Reserpine
W. Rt., Whole root

Occ., Occasional
P, Placebo (treatment column)
G, Genuine
S.D., Standard deviation

n, Degree of freedom (number of observations minus 2)

t, Ratio: $\frac{\text{Difference between means}}{\text{Standard error of difference}}$

P, Probability
c̄, With

TABLE 1—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
8	46 Cauc. F.	N	Narrow c̄ occ. goniosynechias	0	0	Als. 32 mg.	P100-G84-P77	19.9 ±3.85	18.8 ±3.11	32	0.894	>0.3	
9	65 Cauc. F.	N	Wide	0	0	Res. 8.0 mg.	P37-G95-P66	19.4 ±3.72	19.4 ±2.40	27	0.008	>0.9	
10	65 Cauc. F.	N	Wide	0	0	Res. 8.0 mg.	P37-G95-P66	19.2 ±3.06	20.0 ±2.12	27	0.811	>0.4	
11	47 Cauc. F.	N	Wide c̄ occ. goniosynechias	0	0	W. Rt. 300 mg.	P36-G84-P63	20.8 ±3.62	19.8 ±2.49	25	0.853	>0.4	
12	47 Cauc. F.	N	Wide c̄ occ. goniosynechias	0	0	W. Rt. 300 mg.	P36-G84-P63	20.0 ±2.80	20.8 ±1.27	25	0.952	>0.3	
13	84 Cauc. F.	N	—	0	0	Als. 24 mg.	P52-G91-P77	21.7 ±3.57	19.3 ±4.43	26	1.612	>0.1	
14	79 Cauc. M.	N	Wide	0	Pilo.	W. Rt. 1000 mg.	P43-G84-P84	16.0 ±3.33	17.4 ±2.84	26	1.185	>0.2	Prophylactic miotics
15	84 Cauc. F.	N	Wide	0	Pilo.	W. Rt. 1200 mg.	P36-G84-P70-G91-P84-G63	23.3 ±2.74	22.5 ±3.20	62	1.025	>0.3	Prophylactic miotics
16	82 Cauc. F.	N	Wide c̄ occ. goniosynechias	0	0	Als. 16 mg.	P90-G85-P91	20.8 ±2.95	19.0 ±3.25	30	1.564	>0.1	

TABLE 1—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
17	78 Cauc. F.	N	Narrow	0	Pilo.	Als. 24 mg.	P53-G70-P70	19.6 ±3.92	20.6 ±2.22	24	0.761	>0.4	Prophylactic miotics
18	72 Cauc. M.	N	Wide	0	Pilo.	Res. 8.0 mg.	G83-P91-G112-P119-G125-P97	23.6 ±2.95	24.0 ±3.37	82	0.504	>0.6	Prophylactic miotics
19	63 Cauc. F.	?N	Wide	0	0	Als. 24 mg.	P1-G49-P42-G112-P91-G91-P119	26.1 ±4.06	26.0 ±2.70	68	0.139	>0.8	Probably normal in spite of high tension
20	63 Cauc. F.	?N	Wide	0	0	Als. 24 mg.	P1-G49-P42-G112-P91-G91-P119	27.1 ±3.74	28.1 ±2.94	68	1.279	>0.2	Probably normal in spite of high tension.
21	49 Cauc. F.	?N	Wide	0	0	Als. 18 mg.	P16-G91-P84	28.1 ±4.00	27.3 ±2.90	24	0.582	>0.5	Probably normal in spite of high tension.
22	49 Cauc. F.	?N	Wide	0	0	Als. 18 mg.	P16-G91-P84	30.1 ±2.20	27.9 ±4.01	24	1.733	>0.05	Probably normal in spite of high tension.
23	70 Cauc. F.	N	Wide	0	0	Als. 32 mg.	P53-G91-P62	24.6 ±2.58	21.8 ±2.42	27	2.979	<0.01	
24	70 Cauc. F.	N	Wide	0	0	Als. 32 mg.	P53-G91-P62	25.0 ±2.28	21.9 ±2.70	27	3.410	<0.01	

TABLE 2

GROUP II: GLAUCOMATOUS EYES NONRESPONSIVE TO ORAL RAUWOLFIA

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type of Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
25	64 Cauc. M.	C.S.G.	Narrow	Cyclodialysis 1951	0	Als. 32 mg.	P57-G98-P56	14.4 ±2.10	13.4 ±3.29	26	1.003	>0.3	
26	64 Cauc. M.	C.S.G.	Narrow	Cyclodialysis 1950	0	Als. 32 mg.	P57-G98-P56	9.9 ±2.66	9.4 ±2.50	26	0.463	>0.6	
27	83 Cauc. F.	Abs. gl. rubeosis iridis	—	0	Pilo.	Als. 24 mg.	P1-G112-P63-G84-P85	53.5 ±12.18	52.4 ±8.39	36	0.336	>0.7	
28	83 Cauc. F.	C.S.G.	—	0	Pilo.	Als. 24 mg.	P1-G112-P63-G84-P85	23.0 ±4.10	21.6 ±3.48	47	1.376	>0.1	
29	63 Cauc. F.	C.S.G.	Narrow	Cyclodialysis 1950	Pilo.+ Carcholin	Res. 12.0 mg.	P43-G91-P56-G84-P119	22.4 ±2.78	21.8 ±2.86	52	0.805	>0.4	
30	63 Cauc. F.	C.S.G.	Narrow	Cyclodialysis 1950	Pilo.+ Carcholin	Res. 12.0 mg.	P43-G91-P56-G84-P119	23.5 ±3.37	22.1 ±2.20	52	1.738	>0.05	
31	81 Cauc. M.	C.S.G.	Narrow	0	Pilo.	Res. 10.0 mg.	P50-G84-P63	23.0 ±5.56	24.4 ±2.64	24	0.806	>0.4	

Cauc., Caucasian
F., Female
M., Male
C.S.G., Chronic simple glaucoma
Abs. gl., Absolute glaucoma

Hm. 2° gl. ? CRVT hr., Hemorrhage secondary glaucoma possibly due to central retinal vein thrombosis
DFP., Diisopropylfluorophosphate
Pilo., Pilocarpine nitrate
Res., Reserpine

Als., Alseroxylon fraction
&, With
W. Rt., whole root
Occ., Occasional
P, Placebo (treatment column)
G, Genuine

n, Degrees of freedom (number of observations minus 2)
t, Ratio: $\frac{\text{Difference between means}}{\text{Standard error of difference}}$
P, Probability
S.D., Standard deviation
Cat. Extr., Cataract extraction

TABLE 2—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
32	81 Cauc. M.	C.S.G.	Narrow	0	Pilo.	Res. 10.0 mg.	P50-G84-P63	20.5 ±2.47	20.5 ±2.39	24	0.000	>0	
33	79 Cauc. M.	Hm. 2° gl. ? CRVThr.	Closed, 2° to iridiocyclitis	Cyclodia-thermy, April 1953	Pilo.	W. Rt. 1000 mg.	P43-G84-P84	15.4 ±3.90	15.5 ±2.94	26	0.093	>0.9	
34	78 Cauc. F.	C.S.G.	Narrow	0	Pilo.	Als. 24 mg.	P53-G70-P70	24.3 ±3.55	26.1 ±2.38	24	1.452	>0.1	
35	90 Cauc. F.	C.S.G.	—	0	Pilo.	W. Rt. 1200 mg.	P49-G98-P77	21.8 ±2.83	21.0 ±3.57	28	0.694	>0.4	
36	90 Cauc. F.	C.S.G.	—	0	Pilo.	W. Rt. 1200 mg.	P49-G98-P77	21.9 ±3.33	20.9 ±3.59	29	0.871	>0.3	
37	83 Cauc. M.	C.S.G.	Narrow	0	Pilo.	W. Rt. 1200 mg.	P36-G98-P91	25.0 ±3.76	24.5 ±3.76	29	0.338	>0.7	
38	83 Cauc. M.	C.S.G.	Narrow	0	Pilo.	W. Rt. 1200 mg.	P36-G98-P91	24.1 ±3.83	23.6 ±3.78	29	0.317	>0.7	
39	65 Cauc. F.	C.S.G.	Wide	0	Pilo.	W. Rt. 1200 mg.	G91-P105-G126-P49	28.3 ±3.36	26.9 ±3.05	49	1.568	>0.1	
40	65 Cauc. F.	C.S.G.	Wide	0	Pilo.	W. Rt. 1200 mg.	G91-P105-G126-P49	28.6 ±1.75	28.8 ±2.57	49	0.405	>0.6	

TABLE 2—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
41	58 Cauc. F.	C.S.G.	Wide but numerous synechias & many occluded areas	0	Pilo.	Res. 8.0 mg.	P63-G91-P154	26.3 ±1.87	25.3 ±2.43	36	1.306	=0.2	
42	58 Cauc. F.	C.S.G.	Wide but numerous synechias & many occluded areas	0	Pilo.	Res. 8.0 mg.	P63-G91-P154	26.2 ±3.03	25.7 ±2.87	36	0.505	>0.6	
43	77 Cauc. M.	C.S.G.	Narrow	0	Pilo.+ Eserine	Res. 3.0 mg.	P57-G105-P98	41.3 ±6.10	41.1 ±7.24	33	0.095	>0.9	Acetazoleamide throughout observation period
44	77 Cauc. M.	C.S.G.	Narrow ♂ occ. goniosynechias, Cyclodialysis cleft open	Cyclodialysis 1952; Cyclo-diathermy 1953	Pilo.+ Eserine	Res. 3.0 mg.	G92-P105-G105-P98	29.2 ±3.38	29.0 ±6.00	51	0.196	>0.8	Acetazoleamide throughout observation period
45	78 Cauc. F.	Phthisis Bulbi	Narrow	Iridencleisis 1949 for Ac. Cong. Gl.	0	Res. 3.0 mg.	P234-G42-P49-G98-P77-G126-P110-G177	15.5 ±4.19	14.2 >2.49	98	1.969	>0.05	
46	59 Cauc. F.	C.S.G.	Narrow ♂ occ. goniosynechias	0	Pilo.+ Eserine	Als. 12 mg.	P43-G84-P105-G139-P84	26.5 ±3.02	26.4 ±2.67	62	0.108	>0.9	
47	74 Cauc. M.	C.S.G.	Wide	0	Pilo. 1%	Res. 6.0 mg.	P1-G42-P42-G98-P70-G77	26.4 ±5.91	25.9 ±6.20	46	0.318	>0.7	First 330 days; Pilocarpine 1%
					Pilo. 4%	Res. 6.0 mg.	G50-P140-G112	27.0 ±2.60	27.5 ±3.75	41	0.479	>0.6	Last 302 days; Pilocarpine changed to 4%

TABLE 2—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
48	74 Cauc. M.	C.S.G.	Occluded; some rubeosis	0	Pilo. 1%	Res. 6.0 mg.	P1-G42-P42-G98-P70-G77	29.9 ±7.87	28.1 ±9.57	46	0.656	>0.5	First 330 days; Pilocarpine 1%
					Pilo. 4%	6.0 mg.	G50-P140-G112	34.8 ±4.42	31.6 ±5.11	41	2.169	<0.05	Last 302 days; Pilocarpine changed to 4%
49	59 Cauc. F.	C.S.G.	Narrow c occ. goniosynechias	0	Pilo.+ Eserine	Als. 12 mg.	P43-G84-P105-G139-P84	24.6 ±2.65	23.8 ±2.00	62	1.245	>0.2	Crude data
								25.2 ±2.63	23.5 ±2.04	42	2.349	<0.05	1st 5 weeks eliminated from each period except initial placebo period to allow for lag.
50	80 Cauc. M.	C.S.G.	Wide	0	Pilo.	Als. 18 mg.	P93-G105-P147-G112-P98	26.7 ±5.48	25.5 ±3.65	73	1.042	=0.3	Crude data for entire 555-day period.
							P93-G105-P91	29.1 ±6.11	24.2 ±4.07	34	2.442	=0.02	Data for 1st 289 days; 1st 4 weeks of active drug period eliminated (lag effect).
51	84 Cauc. F.	Aphakic G.L.	—	Cat. extr.	DFP	Als. 24 mg.	P52-G91-P77	11.5 ±4.80	9.7 ±3.52	26	1.114	>0.2	Crude data for entire 220-day period.
							P52-G91-	16.8 ±2.56	9.7 ±3.52	16	4.404	<0.001	Final 77-day placebo period omitted (tension remained low).

to 84 estimations of intraocular pressure (n plus 2). There is no indication that the administration of Rauwolfia influenced the prevailing level of intraocular pressure in 22 of the 24 eyes in this group (P greater than 0.05). In the case of two eyes, however (eyes numbered 23 and 24; both from same patient), the level of tension appeared to be significantly lower during treatment with active Rauwolfia than with the placebo (P less than 0.01).

Group II is represented by 27 glaucomatous eyes in 17 patients (table 2). The statistical analyses were based on from 18 to 100 measurements of intraocular pressure. In the case of 23 of the eyes (eyes numbered 25 to 47) there is no apparent significant difference between the mean of the estimations of ocular tension during the placebo and the active drug periods (P greater than 0.05). The remaining four eyes in this group merit separate consideration, however.

Eye number 48 was studied over a total period of 632 days. At approximately the midpoint of this interval the concentration of pilocarpine nitrate was increased from one to four percent. The ocular tension, apparently unaffected by Rauwolfia when one-percent pilocarpine was used, was significantly lowered during treatment with Rauwolfia after the pilocarpine dosage was increased. By contrast eye number 47 (same patient) did not reflect this difference in apparent response when the pilocarpine was changed. This discrepancy is not explained.

Eyes numbered 49, 50, and 51 show no apparent effect on intraocular pressure when the crude data are considered. However, when the data are refined as indicated in Table 2 to allow for a delay in onset or cessation of effect or to eliminate portions of the observation period during which the intraocular pressure did not rise with placebo therapy, significant lowering of the ocular tension by Rauwolfia treatment is uncovered. Although these four eyes are classified in Group II (glaucomatous eyes in which the intraocular pressure is unaffected by Rauwolfia therapy), they are considered as possibly representing examples of responsive eyes.

In Table 3 the third group, consisting of 11 glaucomatous eyes in eight patients, is presented. The analyses were based on from 20 to 100 observations of intraocular pressure. Each eye in Group III appears to present an example of a statistically significant lowering of the mean of numerous estimations of intraocular pressure during prolonged therapy with active Rauwolfia as compared with similar periods of placebo therapy (P less than 0.001 in six eyes; less than 0.02 in three eyes; and less than 0.01 in two eyes). In the case of the six eyes with P values less than 0.001 the data are shown only in their crude form. Were allowance to be made for a lag effect and for spontaneous changes in the severity of the ocular hypertension during the prolonged observation periods the differences between the means would have been more striking. An example of a typical response to alternating courses of placebo and reserpine therapy is illustrated in Figure 1.

The data for eyes numbered 58 to 62 are given both in their crude form and after suitable refinements. With these modifications 10 of the 11 eyes in this group show lowering of intraocular pressure with P values of less than 0.001 while in one eye the P value is less than 0.01.

The clinical implications of a small, but significant, difference between the mean tension during the placebo and active drug periods are, perhaps, more apparent when the data are considered in a somewhat different fashion. In Table 4 the data for eye number 52, a typical example, are arranged to show the relative preponderance of elevated intraocular pressure readings during the placebo periods as contrasted with the preponderance of normal readings during the periods of treatment with alseroxylon fraction. Note that there were a total of 94 observations of ocular tension over a period of 702 days represented by these figures.

TABLE 3

GROUP III: GLAUCOMATOUS EYES RESPONSIVE TO ORAL RAUWOLFIA

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
52	68 Cauc. F.	C.S.G.	Wide	0	Pilo.	Als. 32 mg.	P44-G147-P133-G140-P112-G126	27.6 ±3.32	25.3 ±2.92	92	3.638	<0.001	
53	68 Cauc. F	C.S.G.	Wide	0	Pilo.	Als. 32 mg.	P44-G147-P133-G140-P112-G126	28.2 ±2.97	26.1 ±2.83	92	3.544	<0.001	
54	76 Cauc. M.	C.S.G.	Wide	0	Pilo.	Res. 1.25 mg.	P44-G112-P126-G112-P98-G195	26.3 ±3.56	23.9 ±2.90	86	3.565	<0.001	
55	76 Cauc. M.	C.S.G.	Occluded	0	Pilo.	Res. 1.25 mg.	P44-G112-P126-G112-P98-G195	50.4 ±7.98	39.5 ±7.37	86	6.592	<0.001	
56	78 Cauc. F.	C.S.G.	Narrow	0	Pilo.	Res. 3.0 mg.	P234-G42-P49-G98-P77-G126-P110-G177	29.0 ±4.11	24.8 ±2.68	98	6.241	<0.001	See Figure 1
57	72 Cauc. M.	Abs. gl.	Wide ♂ occ. goniosynechias	Cyclodia-thermy 1952	0	Res. 8.0 mg.	G83-P91-G112-P119-G125-P98	56.9 ±7.09	50.4 ±6.76	82	4.289	<0.001	
58	82 Cauc. F.	Hm. gl. CRVThr.	Wide ♂ gonio-synechias	0	Pilo.	Als. 16 mg.	P90-G85-P91	24.6 ±7.39	19.1 ±2.91	30	2.460	<0.02	Represents data for entire 266-day period while on pilocarpine.
							P90-G85	30.8 ±7.87	19.1 ±2.91	18	4.726	<0.001	See text and fig. 2. The effect is better characterized by eliminating the last placebo period.
59	84 Cauc. F.	Hm. gl. CRVThr.	Occluded; rubeosis iridis	0	Pilo.	W. rt. 1200 mg.	P36-G84-P70-G91-	50.9 ±11.46	44.5 ±8.89	61	2.514	<0.02	Crude data
							P84-G53	50.9 ±11.46	42.5 ±8.50	46	2.784	<0.01	Data refined by eliminating 1st 5 weeks of each drug period to allow for lag effect.

TABLE 3—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Miotics	Rauwolfia: Type & Daily Dose	Sequence of Treatment, Days	Tension, mm. Hg (Mean ± S.D.)		n	t	P	Remarks
								Placebo	Active Drug				
60	80 Cauc. M.	C.S.G.	Wide	0	Pilo.	Als. 18 mg.	P93-G105-P147-G112-P98	24.0 ±3.64	21.6 ±3.24	73	2.865	<0.01	Crude data for entire 555-day observation period.
							P93-G105-P91	25.6 ±3.85	20.2 ±2.86	34	4.206	<0.001	Data for 1st 289 days of observation; 1st 4 weeks of active drug period eliminated (lag).
61	65 Cauc. F.	C.S.G.	Wide	0	Pilo.+ Eserine	Res. 3.0 mg.	P46-G112-P154-G105	28.7 ±4.07	26.4 ±2.39	50	2.519	<0.02	Crude data
								30.1 ±3.61	25.7 ±2.60	32	3.895	<0.001	First 6 weeks of 2nd placebo period and both active drug periods eliminated to allow for lag effect.
62	65 Cauc. F	C.S.G.	Wide	0	Pilo.+ Eserine	Res. 3.0 mg.	P46-G112-P154-G105	29.5 ±3.83	26.6 ±2.28	50	3.334	<0.01	Crude data
								30.6 ±3.58	25.9 ±2.46	32	4.333	<0.001	First 6 weeks of 2nd placebo period and both active drug periods eliminated to allow for lag effect.

Cauc., Caucasian
F., Female
M., Male
C.S.G., Chronic simple glaucoma
Abs. gl., Absolute glaucoma

Hm. gl. CRVT hr., Hemorrhagic glaucoma secondary to thrombosis of central retinal vein
Pilo., Pilocarpine nitrate
Als., Alseroxylon fraction

Res., Reserpine
W. Rt., Whole root
P, Placebo (treatment column)
G, Genuine
S.D., Standard deviation

n, Degrees of freedom (number of observations minus 2)

t, Ratio: $\frac{\text{Difference between means}}{\text{Standard error of difference}}$

P, Probability
c̄, With

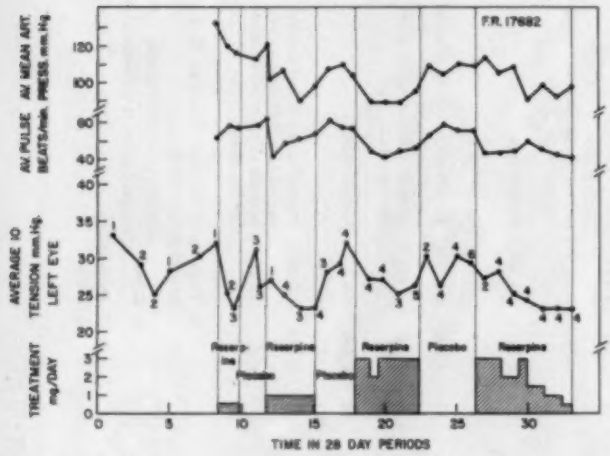

Fig. 1 (Kaplan and Pilger). An example of the typical response of the intraocular pressure, mean arterial pressure (taken as the sum of the diastolic pressure and one third of the pulse pressure), and pulse rate to alternating courses of placebo and reserpine therapy. A 78-year-old Caucasian woman with chronic simple glaucoma, narrow-angle type, left eye. Pilocarpine was used throughout the period of observation without change in concentration or frequency of administration. The data presented here represent a total of 101 observations between May 18, 1953, and December 1, 1955. In the interest of simplicity the data have been condensed by dividing the observation period into 28-day intervals, each point on the curves representing the *average* of the measurements since the end of the preceding interval. The number of observations contributing to each average value plotted is indicated on the curve of intraocular pressure; the same number of measurements of blood pressure and pulse were made. Intraocular pressure during combined placebo periods: 29.0 ± 4.11 mm. Hg; during combined reserpine periods: 24.8 ± 2.68 mm. Hg (mean $\pm$ S. D.); P, less than 0.001.

The Chi-square value[10] lends further support to the significance of the data.

The response of eye number 58 was unique and is therefore presented in more detail.

Case report

An 82-year-old woman developed hemorrhagic glaucoma in the left eye following thrombosis of the central retinal vein. Her filtration angle was wide but there were anterior goniosynechias. She was treated initially with bishydroxycoumarin, miotics, and placebo alseroxylon tablets for 90 days during which time the intraocular pressure was 30.8 ± 7.9 mm. Hg (mean $\pm$ standard deviation). The tension measured 46 mm. Hg at the end of the initial placebo period. One week after therapy with genuine alseroxylon fraction was started, the intraocular pressure was 20 mm. Hg, and during the entire 85-day course of treatment with Rauwolfia remained 19.1 ± 2.91 mm. Hg. Placebo tablets were given for the subsequent 91 days after which the bishydroxycoumarin and miotic therapy was discontinued. The patient was then observed under no therapy other than placebo tablets for another 287 days. In Table 3 the data are shown for the first portion of the observation period when miotic therapy was given. The effect of alseroxylon administration (P less than 0.02) is more accurately characterized, however, when the final placebo period is eliminated (P less than 0.001), for the tension remained 21.7 ± 3.02 mm. Hg (48 observations) during the 378 days after Rauwolfia therapy was stopped (fig. 2).

TABLE 4

THE SIGNIFICANCE OF A "SMALL" DIFFERENCE BETWEEN THE MEANS

Eye 52: Difference between the means		2.3 mm. Hg
Duration of observation period		702 days
Total number of observations		94
Placebo	41	
Drug	53	
Intraocular Pressure	*Placebo*	*Drug*
28 mm. Hg or greater	56.1%	20.8%
25 mm. Hg or less	22.0%	60.4%

Chi-square (based on 27 mm. Hg as dividing line): 12.361
P less than 0.001.

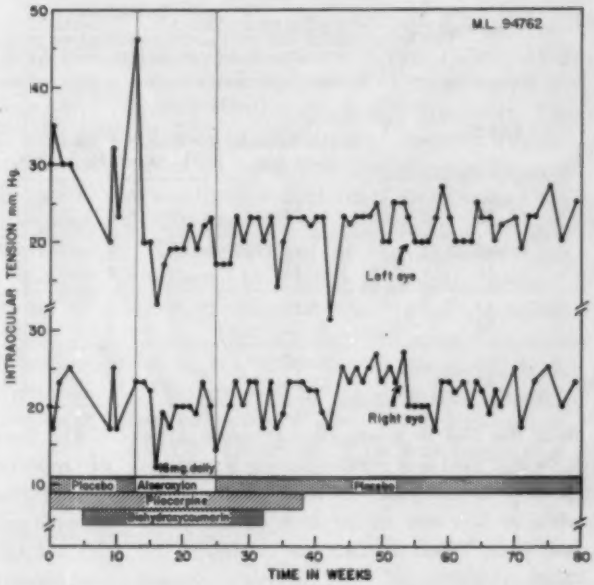

Fig. 2 (Kaplan and Pilger). An 82-year-old Caucasian woman with hemorrhagic glaucoma following central retinal vein thrombosis, left eye; wide angle with anterior goniosynechias. A total of 68 observations are depicted here, covering the period from May 14, 1954, to November 17, 1955. The ocular tension in the affected eye fell from 46 to 20 mm. Hg one week after tablets of the alseroxylon fraction were substituted for placebos and remained normal thereafter even when all forms of therapy other than placebo tablets were stopped. Each point in this graph indicates a single measurement; time intervals, one week (cf. fig. 1). (See text.)

The total experience with long-term oral Rauwolfia therapy is summarized in Table 5.

Discussion

The presence of arterial hypertension does not appear to be a factor in responsiveness of the intraocular pressure to Rauwolfia therapy inasmuch as only two of the 12 responsive patients had a consistently elevated blood pressure (above 90 mm. Hg, diastolic) during placebo periods (eyes numbered 23, 24, 52, and 53) and even in these cases the arterial hypertensive disease was mild.

The nature of the filtration angle does not distinguish the responsive eyes from those in which the ocular tension was apparently unaffected. Although the majority of eyes in the responsive group showed wide angles at gonioscopic examination, narrow-angle glaucoma was also represented as were examples of eyes with completely occluded angles.

Similar types of glaucoma were included in the responsive and the nonresponsive groups.

The response of the intraocular pressure to the ingestion of 1,000 cc. of water following an over-night fast was observed in four patients who had previously been shown to respond to prolonged Rauwolfia treatment. The intraocular pressure was measured before and at 15-minute intervals after the water load for a period of 60 minutes during which the patients remained in a darkened room. Miotics were discontinued from 48 to 72 hours prior to the test. The provocative test was performed twice in each patient: once after a minimum of two months of placebo therapy, and once after a minimum of two months of Rauwolfia administration. The results are summarized in Table 6.

There appears to be no consistent trend

TABLE 5

Long-term oral Rauwolfia therapy

Nonglaucomatous eyes		24 (15 patients)
Responsive	2	
Nonresponsive	22	
Glaucomatous eyes		38 (22 patients)
Responsive	11	
Possibly responsive	4	
Nonresponsive	23	
Total		62 (31 patients)

TABLE 6

THE RESPONSE OF THE INTRAOCULAR PRESSURE TO A STANDARD WATER LOAD: INFLUENCE OF ORAL RAUWOLFIA THERAPY

Eye No.	Placebo		Rauwolfia	
	Initial Tension, (mm. Hg)	Rise in Tension, (mm. Hg)	Initial Tension, (mm. Hg)	Rise in Tension, (mm. Hg)
16	22	1	17	5
58	23	0	17	10
45	12	5	11	9
56	32	8	27	13
52	27	8	37	6
53	27	8	37	6
54	30	16	32	14
55	46	17	46	9

since the rise in intraocular pressure after the water load was greater during Rauwolfia therapy in the case of four of the eyes, while it was less in the case of the other four eyes. When the data are combined, the mean response of the pressure during placebo therapy was a rise of 7.9 mm. Hg (S. D., 6.18), while the mean tension response during Rauwolfia treatment was 9.0 mm. Hg (S. D., 3.30). Although the lack of a significant difference (t, 0.455; P, greater than 0.6) suggests that the depression of intraocular pressure by prolonged oral Rauwolfia administration is not mediated through those processes concerned with the responsiveness of the pressure-regulating mechanisms to a standard water load, this problem will have to be explored in a larger group of patients before the question can be answered.

The maximum tolerated dose of Rauwolfia was used in most instances in order to assure maximum response. As a result many patients noted one or another of the well-recognized pharmacologic effects of these alkaloids. In this particular group of patients excessive bowel motility and lethargy were the most prominent factors limiting dosage. At the conclusion of the period of controlled observation, however, it was possible to lower the dose of Rauwolfia to comfortable levels without loss of effect on ocular pressure.

The lowering of intraocular pressure was of moderate proportions, representing a change from an elevated to a normal level in some patients, while in others the pressure did not fall to the normal range. The effect was, nevertheless, of clinical significance in the total management of a problem in which a combination of methods of treatment may be applicable.

After beginning the administration of the Rauwolfia derivatives an effect on the ocular tension was apparent sometimes within one week; but, in other cases there was a delay of from four to six weeks before the pressure dropped. Similarly, a period of several weeks may elapse after cessation of treatment before the influence of Rauwolfia is entirely dissipated. A therapeutic trial of at least eight weeks' duration might be necessary to determine whether a given eye will respond to Rauwolfia therapy.

PART II: INTRAVENOUS RESERPINE

A. EFFECT ON INTRAOCULAR PRESSURE

Methods. Reserpine was administered intravenously in doses ranging from 73 to 295 μg per kg. to 20 hospitalized patients.* After several estimations of intraocular pressure, blood pressure, and pulse over a period

*Ampuls of reserpine were supplied by Ciba Pharmaceutical Products, Inc. (Serpasil® Injectable Solution).

sufficient to establish a stable control level the reserpine solution, diluted to 10 cc., was injected at the rate of 2.0 cc. per minute. The intraocular pressure, blood pressure, and pulse were measured at 30-minute intervals for the first two to three hours after the injection, at one- to two-hour intervals until 12 to 16 hours after administration of the drug, and at four- to six-hour intervals thereafter until the level of ocular tension had returned to the baseline. The 40 eyes are divided into two groups, each consisting of 20 eyes: Group I includes the eyes with baseline tensions of less than 30 mm. Hg; Group II consists of the eyes with baseline intraocular pressures of 30 mm. Hg or greater.

Results. The effect of intravenous reserpine in the normotensive eyes (Group I) is summarized in Table 7. This group of 20 eyes is distributed among 20 patients. The influence of intravenous reserpine was observed on more than one occasion in some cases; therefore, 25 trials are tabulated for the 20 eyes.

Twenty-two out of the 25 trials were manifested by a fall in intraocular pressure, the mean change in pressure being a fall of 5.3 mm. Hg (standard deviation, 4.35 mm. Hg; n, 24; "t," 6.063; P, less than 0.001).

The response of the eyes with elevated baseline tension (Group II) is indicated in Table 8. There are 18 patients represented

TABLE 7

INTRAVENOUS RESERPINE

GROUP I: BASELINE TENSION LESS THAN 30 MM. HG

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Dose (μg./Kg.) Route	Intraocular Pressure (mm. Hg)		Remarks
						Baseline	Lowest Level After Drug	
1	84 Cauc. F.	N	Wide	0	133 IV	22	22	
2	80 Cauc. F.	C.S.G.	Narrow c̄ gonio-synechias	Iridectomy for glaucoma 1936; Cataract extraction later	109 IV twice; 9 hours between doses	20	10	7/6/54
					218 IV; 109 IM 8 hours later	16	10	11/17/54
					218 IV	16	12	1/19/55
3	83 Cauc. F.	C.S.G.	Wide	0	88 IV thrice in 7¾ hours	16	10	
4	77 Cauc. M.	N	Wide	0	111 IV	22	17	
5	72 Cauc. M.	N	Wide	0	73 IV	19	17	10/6/54
					146 IV	21	16	10/11/54

Cauc., Caucasian
F., Female
M., Male

N, No evidence of glaucoma
C.S.G., Chronic simple glaucoma
IV, Intravenously

IM, Intramuscularly
c̄, With

TABLE 7—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Dose (μg./Kg.) Route	Intraocular Pressure (mm. Hg)		Remarks
						Baseline	Lowest Level After Drug	
6	81 Cauc. M.	C.S.G.	Narrow	0	158 IV; 79 IV at 5 hours; 79 IM at 23 hours.	23	12	10/28/54
					198 IV	23	12	11/8/54
7	58 Negro M.	N	Wide & few gonio-synechias	0	172 IV; 86 IM	21	19	
8	32 Cauc. M.	N	Wide	0	220 IV	12	19	12/2/54
					220 IV	12	14	12/8/54
9	52 Cauc. F.	N	Wide & many gonio-synechias	0	170 IV	17	10	
10	32 Cauc. F.	C.S.G.	Narrow	0	295 IV	26	20	
11	69 Cauc. F.	N	—	0	176 IV	19	17	
12	72 Cauc. F.	N	Narrow	0	242 IV	22	12	
13	65 Cauc. M.	N	—	0	275 IV	20	8	
14	56 Cauc. M.	N	—	0	194 IV	16	13	
15	69 Cauc. M.	N	Narrow	0	254 IV	20	12	
16	75 Cauc. F.	N	—	0	294 IV	22	14	
17	68 Cauc. M.	N	—	0	167 IV	18	10	
18	68 Cauc. M.	N	—	0	167 IV	17	12	
19	46 Cauc. F.	C.S.G.	—	0	152 IV	24	20	
20	46 Cauc. F.	C.S.G.	—	0	152 IV	26	20	

TABLE 8

INTRAVENOUS RESERPINE

GROUP II: BASELINE TENSION 30 MM. HG OR GREATER

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Dose (μg./Kg.) Route	Intraocular Pressure (mm. Hg)		Remarks
						Baseline	Lowest Level After Drug	
2	80 Cauc. F.	C.S.G.	Narrow c̄ gonio-synechias	Iridectomy for glaucoma 1936; Cataract extraction later	109 IV twice in 4 hours	30	10	
21	84 Cauc. F.	Hm. gl.-CRVThr.	Occluded; rubeosis iridis	0	133 IV	55	48	
22	80 Cauc. F.	C.S.G.	Narrow c̄ gonio-synechias; mild rubeosis iridis	Iridencleisis 1932; Cataract extraction later	109 IV twice 9 hours	39	12	7/6/54. Tension *began* to return toward baseline 27 hours after 1st dose in spite of repeated injections.
					109 IV twice in 4 hours	46	16	8/24/54. Tension *began* to return toward baseline 21 hours after 1st dose in spite of repeated injections.
					218 IV; 109 IM in 8 hours	63	22	11/17/54. Given night before surgery—normotensive eye in morning at time of cyclodialysis.
					218 IV	37	25	1/19/55. Given night before surgery (cyclodialysis).
23	83 Cauc. F.	Ac. cong. gl.	Wide	0	88 IV thrice in 7½ hours	52	27	
24	77 Cauc. M.	Ac. cong. gl.	Wide c̄ few gonio-synechias	0	111 IV	67	26	Pain disappeared. Tension *began* to return toward baseline between 24 and 48 hours after 1st dose in spite of additional injections.
25	72 Cauc. M.	Abs. gl.	Wide c̄ occ. gonio-synechias	Cyclo-diathermy 1952	73 IV	53	43	10/6/54.
					146 IV	48	32	10/11/54. Response to Acetazoleamide, 500 mg., was similar.
26	81 Cauc. M.	C.S.G.	Narrow	0	158 IV; 79 IV at 5 hours; 79 IM at 33 hours.	32	17	10/28/54. Tension *began* to return toward baseline 29 hours after 1st dose in spite of additional injections.
					198 IV	34	17	11/8/54. Before maximum effect, norepinephrine infusion elevated blood pressure *well above* and intraocular tension *just to* baseline.
27	58 Negro M	Abs. gl., cong.	Occluded	0	172 IV; 86 IM	55	43	Intensive miotic treatment subsequently had no effect.
28	77° Cauc. F.	Abs. gl., Hm.—CRVThr.	Occluded; rubeosis iridis	Cyclo-diathermy 2/54 & 3/54	249 IV	68	21	Norepinephrine infusion raised blood pressure to baseline but ocular tension remained down (See fig. 4).
29	77 Cauc. F.	N	Narrow c̄ few gonio-synechias	0	249 IV	32	20	
30	32 Cauc. M.	Ac. cong. gl. 2° to vascularization of angle	Occluded due to Rubeosis Iridis	0	220 IV	100	22	12/2/54. Diabetes mellitus c̄ severe nephropathy. Pain and corneal edema disappeared at peak of effect. Repeated doses did not prevent beginning elevation of tension 35 hours after 1st injection. (See fig. 3).
					220 IV	79	29	12/8/54. Subsequently several surgical procedures only partially controlled the ocular hypertension.

Cauc., Caucasian
F., Female
M., Male
C.S.G., Chronic simple glaucoma
Hm. gl. CRVThr., Hemorrhage glaucoma secondary to thrombosis of central retinal vein
Ac. cong. gl., Acute congestive glaucoma
Abs. gl., Absolute glaucoma
Abs. gl. cong., Absolute glaucoma congestive
N, No evidence of Glaucoma
Ac. cong. gl. 2°, Acute congestive glaucoma secondary to
Abs. gl. hm. CRVT hr., Absolute glaucoma, hemorrhagic, secondary to thrombosis of Central Retinal Vein
c̄, With
IV, Intravenously
IM, Intramuscularly

TABLE 8—(*continued*)

Eye	Age Race Sex	Diagnosis	Gonioscopy, Angle	Previous Ocular Surgery	Dose (μg./Kg.) Route	Intraocular Pressure (mm. Hg)		Remarks
						Baseline	Lowest Level After Drug	
31	52 Cauc. F.	Abs. gl.	Occluded	0	170 IV	39	21	Intraocular pressure remained down when blood pressure was elevated to baseline by norepinephrine infusion. Miotics later failed to control tension.
32	32 Cauc. F.	Ac. cong. gl.	Narrow	0	295 IV	79	35	Later intensive treatment with miotics and acetazoleamide did not lower tension below 35 mm. Hg. Iridencleisis with anterior sclerectomy on 3rd day with good result.
33	69 Cauc. F.	Ac. gl. 2° to intumescent lens	—	0	176 IV	65	48	Subsequently no response to miotics. Cataract extraction on 2nd day with good result.
34	72 Cauc. F.	Ac. cong. gl.	Narrow	0	242 IV	96	10	Intraocular tension remained normal when blood pressure was elevated to baseline by norepinephrine infusion. Tension fell to 6 mm. Hg after the infusion was stopped. Miotics were started 36 hours after the reserpine injection. Tension reached 27 mm. Hg on 7th day. Iridencleisis on 8th day.
35	65 Cauc. M.	Gl. 2° to pupillary block	—	0	275 IV	40	25	Norepinephrine infusion started when reserpine was injected. Both blood pressure and ocular tension remained stationary during the 6-hour infusion. Ocular tension fell within 1 hour after infusion stopped. Pulmonary emphysema: required 3 doses of epinephrine, 1:1000, 0.5 c.c., for severe bronchospasm during infusion period. Iridectomy and cyclodialysis at 24 hours with ocular and arterial tensions still down.
36	43 Negro F.	Ac. cong. gl.	Occluded c numerous gonio-synechias	0	216 IV	86	48	Norepinephrine infusion started when reserpine was injected. Blood pressure was maintained at baseline for 5 hours with only slight fall in intraocular tension. Ocular tension fell within 30 minutes after infusion stopped. At time of maximum effect patient became uncooperative; compressed lids during tension measurements. Ocular tension probably actually fell to lower level than indicated.
37	43 Negro F.	C.S.G.	Occluded c numerous gonio-synechias	0	216 IV	46	26	See remarks, eye 36.
38	56 Cauc. M.	Gl. 2° to uveitis, possibly phakogenic	—	0	194 IV	63	35	Norepinephrine infusion started when reserpine was injected. Blood pressure drop was prevented for 5 hours with moderate fall in ocular tension. Precipitous fall in ocular pressure within 30 minutes after infusion stopped; within 1 hour severe pain disappeared. Subsequently treated with homatropine and intravenous typhoid vaccine (for uveitis) after failure of miotics.
39	69 Cauc. M.	Ac. cong. gl.	Narrow c many gonio-synechias	0	254 IV	51	17	Norepinephrine infusion prevented sustained blood pressure drop for 6 hours 20 minutes with moderate drop in ocular pressure. Ocular tension fell to normal within 80 minutes after end of infusion. Miotics had only slight transient effect. 60 hours after 1st dose a 2nd injection of reserpine only lowered tension from 55 to 40 mm. Hg over night. Iridencleisis on 4th day.
40	75 Cauc. F.	Ac. gl. 2° to intumescent lens	—	0	294 IV	80	25	No response to intensive treatment with 6% pilocarpine (tension actually rose). Intravenous reserpine lowered tension to normal with complete relief of pain. Cataract extraction at normal ocular tension with good result.

TABLE 9

INTRAVENOUS RESERPINE

Eyes with control tension below 30 mm. Hg	20 (20 patients)
Change in intraocular pressure	-5.3 ± 4.35 mm. Hg
Ratio $\frac{\text{Change in intraocular pressure}}{\text{Change in mean arterial pressure}}$	0.15
Eyes with control tension 30 mm. Hg or greater	20 (18 patients)
Change in intraocular pressure	-30.2 ± 20.13 mm. Hg
Ratio $\frac{\text{Change in intraocular pressure}}{\text{Change in mean arterial pressure}}$	0.83
Total	40 (20 patients)

by these 20 eyes. In some instances the effect of intravenous reserpine was observed on more than one occasion so that 27 trials are tabulated for the 20 eyes. In one instance (eye number 2) the baseline tension was normal on three occasions and 30 mm. Hg on one trial; the former data are included in Group I and the latter in Group II.

In every trial the intravenous administration of reserpine was followed by a fall in intraocular pressure varying from 7.0 to 86 mm. Hg, with a mean drop of 30.2 mm. Hg (standard deviation, 20.13; n, 26; "t," 7.791; P, less than 0.001). In 19 trials the intraocular pressure was lowered to levels below 30 mm. Hg.

The "mean" blood pressure, taken as the sum of the diastolic pressure plus one third of the pulse pressure, averaged 103.0 mm. Hg during the baseline observation period; at its lowest level after the injection the "mean" blood pressure averaged 66.4 mm. Hg, an average fall of 36.6 mm. Hg (table 9).

The dynamics of the response of the intraocular pressure were the same in both Group I and Group II. In Table 10 the time from the injection until the first detected effect, the maximum detected effect, and the first detected tendency to return toward the baseline is indicated for both the ocular and the mean arterial pressure. Eye number 34 was atypical in that there was no tendency to elevation of intraocular pressure for seven days after the injection; if this datum was included the average number of hours until the first detected tendency to return toward the baseline would be 30.5 (range 6.0 to 168). The data shown in Table 10 more nearly characterize the usual response, however.

Discussion. Early in the course of the

TABLE 10

DYNAMICS OF RESPONSE OF INTRAOCULAR PRESSURE AND MEAN ARTERIAL PRESSURE TO THE INTRAVENOUS INJECTION OF RESERPINE*

	First Detected Effect, Hours after Injection	Maximum Detected Effect, Hours after Injection	First Detected Tendency to Return toward Baseline, Hours after Injection
Intraocular Pressure	1.8 (0.5–4.5)	8.7 (1.3–25.5)	23.9† (6–48)
Arterial Pressure	1.5 (0.5–3.0)	5.9 (1.3–25.5)	12.9 (4–29)

* Figures represent average number of hours from the time of the injection to the indicated manifestation. Figures in parentheses show the range of time-intervals observed.

† Eye 34 excluded; see text.

study there was an attempt in five instances to maintain the intraocular pressure at normal levels by repeated injections of reserpine. It was found uniformly that repeated doses after the initial fall in ocular pressure did not prevent the gradual return of the tension to baseline levels. Responsiveness of the intraocular pressure returned after an interval of approximately one week (fig. 3). The basis for this temporary resistance to the effect of intravenous reserpine is not clear; but, recent studies[5-8] relating the action of reserpine to the release of serotonin might throw some light on this problem. It was shown that the injection of reserpine is followed by a sharp fall in the concentration of serotonin in brain, intestinal tract, and platelet depots and a rise in the amount of 5-hydroxyindoleacetic acid excreted in the urine. Although reserpine was no longer detectable fluorometrically in brain 12 hours after administration, the pharmacologic effects persisted much longer, as did the changes in serotonin concentration and sero-

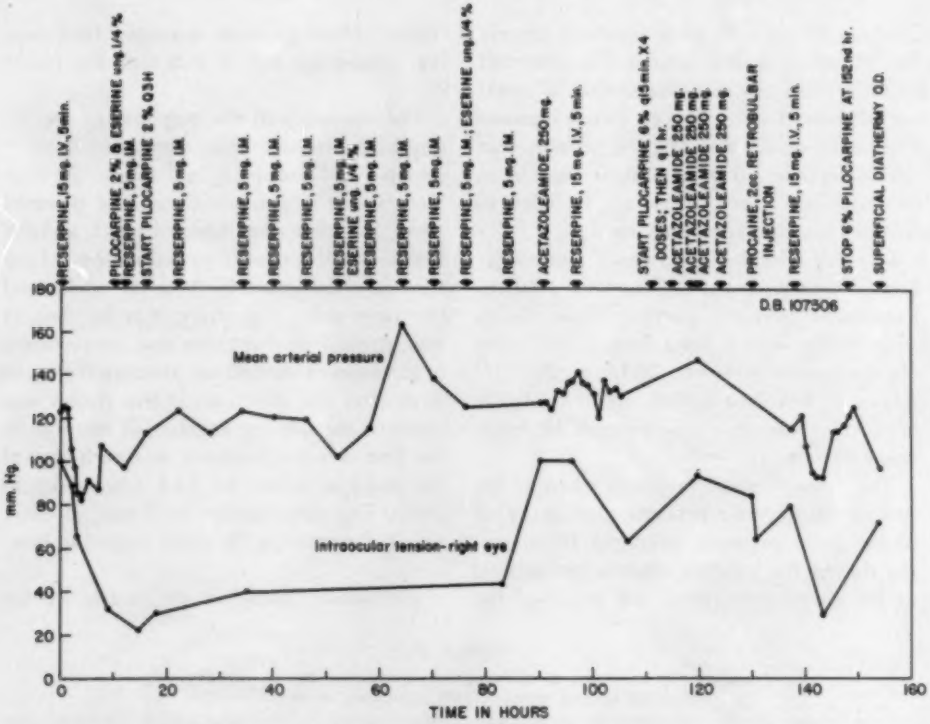

Fig. 3 (Kaplan and Pilger). A 32-year-old Caucasian man with diabetes mellitus and advanced nephropathy. Hospitalized 48 hours after the onset of excruciating pain in the right eye, nausea, and vomiting. Acute congestive glaucoma; angle occluded because of neovascularization of the iris; severe corneal edema; pupil dilated (8.0 mm.) and unresponsive. A single intravenous injection of reserpine, given as the initial form of therapy, was followed by a progressive fall in intraocular pressure from 100 to 22 mm. Hg over a period of 12 to 15 hours (note the proportionately small drop in arterial pressure) together with resolution of corneal edema, disappearance of pain, and constriction of the pupil. Note failure of repeated doses of reserpine, beginning 12 hours after the first injection, to prevent the subsequent rise in intraocular pressure in spite of concomitant miotic therapy. Acetazoleamide administration and a retrobulbar injection of procaine were ineffective. Just 138 hours (5.75 days) after the first reserpine injection, another dose was followed by a prompt drop in ocular tension. Pain was subsequently fairly well controlled after several surgical procedures. Eye remained totally blind.

tonin-metabolite excretion. The level of serotonin in the depots gradually rose to original concentrations over a period of five to seven days after the administration of reserpine. The time needed for replenishment of serotonin levels in brain is similar to the period during which intravenous reserpine is relatively ineffective against the ocular tension. It is interesting to speculate that the ability of intravenous reserpine to lower intraocular pressure might be correlated in some way with the concentration of serotonin in certain midbrain centers.

The development of tolerance to further injections is of importance in the application of intravenous reserpine in the treatment of glaucoma. In order best to exploit the ability of intravenous reserpine to depress the ocular tension it is essential to select the time of administration of the alkaloid with care. A properly timed injection of reserpine in acute glaucoma is likely to make it possible for surgery to be performed on an eye with normal or nearly normal tension. On the average, in such circumstances, the reserpine should be injected approximately eight hours prior to the anticipated time of surgery. On the other hand early administration of intravenous reserpine might lower tension, relieve corneal edema, relieve pain, and restore the responsiveness of a dilated, fixed pupil to miotic agents. If clinical judgment indicates the probability that control of the ocular hypertension can be maintained by standard nonsurgical measures once these salutory effects have been achieved, then the use of this agent should be considered early in the course of the attack.

The fact that there were two instances of acute glaucoma secondary to an intumescent lens, one case of glaucoma due to pupillary block, and seven eyes with occluded filtration angles because of either adhesions or vascularization suggests that the effect of intravenous reserpine in depressing the intraocular pressure is not dependent upon the integrity of the aqueous outflow apparatus.

Conclusions regarding the most suitable dosage range for intravenous reserpine cannot be derived from these data inasmuch as large doses of the drug were utilized in all but the first few patients in the series. The range from 35 to 150 μg. per kg. should be explored, and the effectiveness of the intramuscular route of administration should be studied.

B. Relationship between intraocular and arterial pressure changes

The relationship between the effect of intravenous reserpine on the intraocular pressure and the arterial blood pressure requires comment. It is noteworthy that, on the average, the maximum lowering of the blood pressure occurred 2.8 hours prior to the maximum lowering of the ocular pressure; and, the first detectable rise in blood pressure was noted, on the average, 11.0 hours prior to the first detectable rise in intraocular pressure (table 10). Is the lowering of the intraocular pressure dependent upon the lowering of the arterial blood pressure?

Methods and Results. In a group of four individuals (eight eyes) who were not receiving any medication, the mean arterial pressure was varied by means of an infusion of norepinephrine and the ratio of the change in intraocular pressure to the change in mean arterial pressure calculated (table 11). The mean response ratio was 0.19 (standard deviation, 0.059). The ratio of the average drop in ocular tension to the average fall in arterial pressure in Group I (table 7; normal baseline tensions) was 0.15, a remarkably similar value. Both of these ratios resemble the response ratio of 0.1 described in experimental animals.[11] By contrast the response ratio in Group II (table 8; elevated baseline tensions) was notably higher, 0.83.

In an effort to isolate the blood-pressure response from the ocular-tension response an intravenous infusion of norepinephrine was administered to four patients five, seven, eight, and 18 hours after the injection of

TABLE 11

RATIO OF CHANGE IN INTRAOCULAR PRESSURE TO CHANGE IN MEAN ARTERIAL PRESSURE INDUCED BY AN INTRAVENOUS INFUSION OF NOREPINEPHRINE

Eye No.	Number of Responses Observed	Average Response Ratio
1	4	0.28
2	4	0.25
3	7	0.10
4	7	0.18
5	4	0.18
6	4	0.13
7	5	0.21
8	5	0.19

Mean response ratio: 0.19
Standard deviation: 0.059

reserpine for periods of 100, 57, 78, and 107 minutes respectively (eyes numbered 26, 28, 31, and 34). It was assumed that any change in intraocular pressure during the administration of norepinephrine would reflect a corresponding change in systemic arterial pressure.[11] In the case of eye number 26 the infusion was started before the maximum effect on the intraocular pressure had been achieved and at a time when the mean arterial pressure had already spontaneously returned to the baseline.

The norepinephrine infusion elevated and maintained the mean arterial pressure 36.7 mm. Hg *above* the baseline (average of 20 observations) while the ocular tension rose almost exactly to the baseline (35.4 mm. Hg as compared with the control level of 34 mm. Hg). At the time of apparent maximum effect of the reserpine, 8.5 hours after the injection and two hours after the conclusion of the norepinephrine infusion, the mean arterial pressure was 8.0 mm. Hg below the baseline while the intraocular pressure was 17 mm. Hg below the control value.

The norepinephrine infusion was given after the ocular tension of eyes numbered 28, 31, and 34 had been nearly maximally depressed. The blood pressure was elevated and maintained as closely at the control level as possible. In these patients the ocular tension fluctuated only a few mm., remaining in the normal range throughout the infusion period despite the return of the mean arterial pressure to the baseline (fig. 4).

In four patients an infusion of norepinephrine was started simultaneously with the injection of reserpine. The rate of infusion was adjusted so as to maintain the arterial pressure (estimated at five-minute intervals) at its original level for periods of from five to 6.3 hours. In one of these cases (eye number 35) the intraocular pressure did not fall until shortly after the infusion was discontinued, when both the intraocular pressure

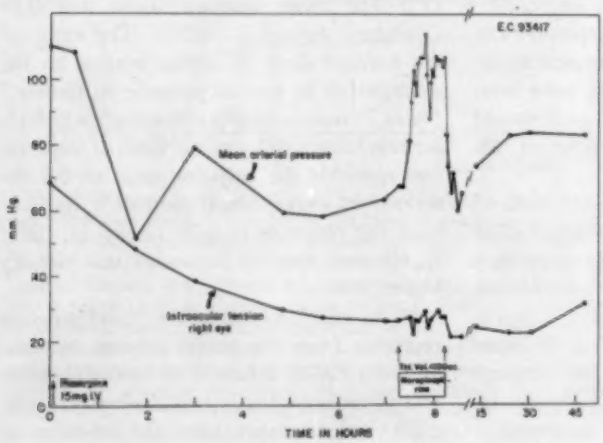

Fig. 4 (Kaplan and Pilger). A 77-year-old Caucasian woman with absolute glaucoma (hemorrhagic) secondary to old central retinal vein thrombosis, right eye; angle occluded, rubeosis iridis. At the height of the effect of intravenous reserpine on the intraocular pressure the blood pressure was elevated approximately to the baseline by means of an infusion of norepinephrine; the intraocular pressure remained normal. This dissociation between the ocular and the arterial pressure responses was observed in three of four patients studied in this manner; in the fourth patient the arterial pressure had to be raised substantially above the control level in order to return the ocular tension to the baseline.

and the blood pressure promptly fell. In one case (eyes numbered 36 and 37) there was a slight fall in intraocular pressure during the period of the infusion and a further prominent drop within 30 minutes after the conclusion of the norepinephrine administration. The remaining two cases (eyes numbered 38 and 39) showed a moderate depression of the ocular tension during the infusion and an additional abrupt decline in pressure 30 and 80 minutes, respectively, after the end of the period of norepinephrine therapy (fig. 5).

Discussion. The observation that the depression of ocular tension was prevented, at least to a considerable extent, when the mean arterial pressure was supported by norepinephrine tends to implicate the primary importance of arterial pressure changes in the response of the intraocular pressure to intravenous reserpine. On the other hand, the appreciably greater ratio of the change in ocular tension to the change in mean arterial pressure in Group II (elevated tension) as compared with the response ratio of Group I (normal tension) and of the group of individuals given norepinephrine without reserpine (table 11) suggests that factors beyond those concerned with the blood pressure change were operative in the case of the eyes with elevated baseline tension. Similarly, the failure to elevate the ocular tension to the baseline with a norepinephrine infusion unless the arterial pressure was raised substantially above the control level could be explained on the basis that intravenous reserpine has a fundamental effect on the intraocular-pressure regulating systems independent of its effect on arterial pressure.

Summary and Conclusions

1. The effect of the administration of alternating courses of placebo and Rauwolfia serpentina preparations over prolonged periods was studied in both normal and glaucomatous eyes of various types. The intraocular pressure was moderately, but significantly, lower during periods of treatment with Rauwolfia tablets than during periods of placebo therapy in two out of 24 nonglaucomatous eyes and in 11 (possibly 15) out of 38 eyes with glaucoma.

2. The response of the intraocular pressure to the intravenous injection of reserpine was observed in 20 normotensive eyes and

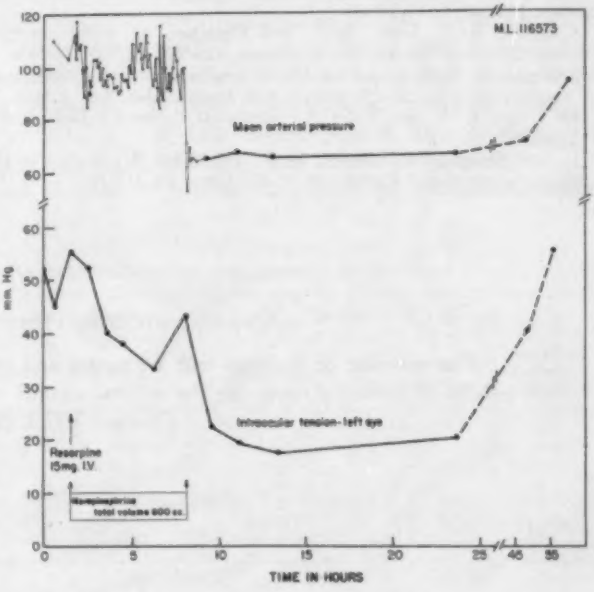

Fig. 5 (Kaplan and Pilger). A 69-year-old Caucasian man with acute congestive glaucoma, narrow-angle, with many peripheral goniosynechias. An intravenous infusion of norepinephrine was administered in an effort to maintain the arterial pressure near the original level for a period of 6.3 hours after the injection of reserpine. Note the moderate drop in intraocular pressure during the infusion period followed by the striking fall to normal levels shortly after the cessation of the norepinephrine infusion. In four patients studied in this fashion the expected fall in ocular tension was either partially (three patients) or entirely (one patient) prevented until shortly after the intravenous infusion of norepinephrine was stopped.

20 eyes with elevated ocular tension associated with various types and stages of glaucoma. The administration of reserpine by the intravenous route was followed by a significant depression in intraocular pressure in 22 out of 25 trials in the normotensive group (change in tension, -5.3 ± 4.35 mm. Hg) and in 27 out of 27 trials in the case of the eyes with high initial tension (change in tension, -30.2 ± 20.13 mm. Hg).

3. The relationship between the response of the intraocular pressure and the arterial pressure following intravenous reserpine was explored by means of the infusion of norepinephrine. Evidence was derived which suggests that, although the fall in intraocular pressure after intravenous administration of reserpine is probably secondary to the drop in arterial pressure in normotensive eyes, mechanisms distinct from those concerned with the arterial pressure response are probably operative in the case of eyes with elevated ocular tension.

4. These observations warrant further study with particular respect to the problems of dosage, mode of action, means of selecting responsive patients, and clinical applicability.

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OPHTHALMIC MINIATURE

The embrace of maidens that are pretty and well shaped relieves the chills of fever, by imparting the natural warmth of their body.

Charaka, VI: 3, 208 (circa 200 A.D.).

OCULAR COMPLICATIONS OF RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS*

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The association of various ocular lesions with inflammatory joint disease has long been recognized. In the earlier literature this recognition was based on neither an exact classification of the ocular inflammation nor the specific etiology of the articular disorder. In recent years, due primarily to the awakening interest in collagen disease, more exact studies of the ocular complications of rheumatic fever, rheumatoid arthritis, and other collagen diseases have appeared. However, in many of these studies the inclusion of such conditions as Reiter's disease, the Stevens-Johnson syndrome, gonococcal arthritis, gout, and other diseases unrelated to rheumatic fever and rheumatoid arthritis, has somewhat clouded the picture of the ocular manifestations of these two entities. When these various unrelated forms of joint disease are excluded, the main information to be gleaned from the literature may be summarized.

Among the older authorities Moore[1] (1912) and deSchweinitz[2] (1917) state that acute (presumably nongranulomatous) iritis either does not occur at all in rheumatic fever, or does so only with the greatest rarity. On the other hand, they clearly recognized the association of such iritis with rheumatoid arthritis. Later observers, Franceschetti[3] (1946), Berens[4] (1950), Vail[5] (1951), David[6] (1953), and Igersheimer[7] (1953), have confirmed the earlier views of Moore and deSchweinitz. In support of these repeated clinical observations, there are various statistical studies by different investigators. These are tabulated in Table 1.

It is immediately evident from this table that, with the single exception of Godtfredsen,[14] it is agreed that uveitis rarely if ever appears as a complication of rheumatic fever. Godtfredsen's report of a four to five percent incidence of iritis in this disease is open to question. This figure is apparently based on an estimate from the experiences of various Scandinavian clinics. The number of cases on which this estimate is based is not given, nor are the sources from which they originated. In view of the diametrically opposed reports from all other investigators and the absence of supporting documentary evidence, Godtfredsen's reported incidence of four to five percent iritis in rheumatic fever may well be held *sub judice*.

On the other hand, the definite occurrence

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital.

TABLE 1

INCIDENCE OF UVEITIS IN RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS

Author	Rheumatic Fever		Rheumatoid Arthritis		
	No. Cases	% Uveitis	No. Cases	% Uveitis in Generalized	% Uveitis in Marie-Strumpell
Coburn[8] (1931)	162	0.3	—	—	—
Berens[9] (1942)	22	0.0	83	2.4	Not given
Mylius[10] (1942)	250	0.0	—	—	—
Rudolph[11] (1945)	105	0.0	—	—	—
Sorsby[12] (1946)	147	0.0	332	4.5	5.7
Mills[13] (1948)	—	—	600	7.0	Not given
Godtfredsen[14] (1949)	Not given	4.5	Not given	2.5–5.0	15–50

of iritis in association with rheumatoid arthritis is clearly evident. The description of this iritis reveals it is invariably of the nongranulomatous type, which recent investigations[15] indicate is usually due to a bacterial hypersensitivity. In order to study further the incidence of such uveitis in rheumatic fever and rheumatoid arthritis, the histories of 200 cases of rheumatic fever and 465 cases of rheumatoid arthritis seen in The Johns Hopkins Hospital have been reviewed. Each of these histories contains a note by the intern, assistant resident, and the physician-in-charge concerning any positive history of ocular inflammation or the presence of any obvious ocular abnormality. With few exceptions, the patients with such positive histories or findings were referred for detailed ophthalmologic examination. The incidence of ocular complications here reported for the entire group of both the rheumatic fever and the rheumatoid arthritis patients is based on the results of these complete ophthalmologic examinations. This statistical approach may give figures which are too low for the entire series, since occasional cases may have been missed by the medical staff and not referred for ophthalmologic examination.

Rheumatic fever

Material

In the period between 1946 and 1952, there were 1,480 patients classified in the medical files of The Johns Hopkins Hospital as having some form of rheumatic fever. In the 1950-1951 period there were 242 such patients. The histories of this latter group were selected for review; 200 of these fully fulfilled Jones'[16] criteria for a positive diagnosis of rheumatic fever; that is, any combination of major manifestations (carditis, arthritis, chorea, nodules, verified history of rheumatic fever), or one of the major and two of the minor manifestations (fever, abdominal or precordial pain, erythema marginatum, epistaxis, pulmonary change, or positive laboratory findings).

Ocular findings

In this group of 200 consecutive patients, selected on the above criteria, 68 percent were females and 32 percent males; 66 percent were white and 34 percent were Negroes. Fifty-one or 25 percent of these patients were referred for ophthalmologic examination, while in 149 the only eye notes available are those of the medical staff. In this latter group (149 cases), various minor unrelated ocular findings were noted in 44 instances. These were such conditions as distended, tortuous retinal veins in mitral stenosis, an occasional hypertensive retinopathy, and so forth. In the 51 patients receiving detailed ophthalmologic examinations, there were 12 instances of positive findings. These were as follows:

Scleritis	1
Granulomatous uveitis	1
Chorioretinal scarring	1
Roth spots	2
Conjunctival splinter hemorrhages	3
Ocular manifestations of cerebral embolism	4

The patient with granulomatous uveitis developed the ocular inflammation 32 years after an isolated attack of acute rheumatic fever. There appeared to be no possible cause-and-effect relationship between the two. The Roth spots noted in two cases of subacute bacterial endocarditis complicating rheumatic fever may well be similar in appearance to the lesions of "focal choroiditis" noted by some observers in this disease.[17]

There was not one single case of acute nongranulomatous iritis in this entire group or any history of residua of such.

Rheumatoid arthritis

For the period between January 1, 1946, and March 31, 1952, there are 578 clinical histories of patients with various forms of probable rheumatoid arthritis in the files of The Johns Hopkins Hospital. On review of these histories, 113 were discarded as not fulfilling the following criteria: (1) a typical clinical history, with physical findings confirmed in most instances by more than one observer; (2) exclusion of cases with

roentgenologic evidence of other joint disease; (3) clinical evidence of other arthritides (as brucella, gonococcal, Reiter's syndrome, Stevens-Johnson syndrome, gouty arthritis, or autopsy findings of other collagen disease).

Of the 465 cases remaining, 57 percent were female and 43 percent male, a smaller female preponderance than the usually quoted 3:1 ratio.

Ninety-one percent were white and nine percent Negro—a smaller percentage than would be expected from the usual 68:32 ratio of white and Negro population in The Johns Hopkins Hospital. Forty percent of these 465 patients had generalized arthritis, 54 percent had local joint involvement, six percent had Marie-Strumpell disease. When classified for the severity of the arthritis, 13 percent were mild, 53 percent moderate, and 34 percent severe. Seventy-seven (16.7 percent) of these patients, on account of a positive ocular history, obvious ocular pathologic process, or occasionally for some other reason, were referred to the Ophthalmology Department for consultation. From the results of these examinations, the percentage incidence of ocular complications in the entire group is calculated. The various ocular complications are shown in Table 2.

Thus, in 465 cases of rheumatoid arthritis occurring in The Johns Hopkins Hospital between 1946 and 1952 there were 29 patients with clearly defined ocular lesions, an over-all incidence of 6.2 percent. As mentioned previously, this figure is almost certainly on the conservative side, as occasional ocular abnormalities may have been missed by the medical consultants and such patients would not have been referred for ophthalmologic examination. Certain of the established ocular complications (table 2) deserve further consideration and comment.

TABLE 2

OCULAR COMPLICATIONS OF RHEUMATOID ARTHRITIS

	No. of Cases	% of Total Group
Nongranulomatous uveitis	16	3.7
Keratitis	6	1.3
Chrysosis corneae	1	.2
Hypervitaminosis D	2	.4
Episcleritis	2	.4
Episcleritis and scleritis	1	.2
Scleromalacia perforans	1	.2
	29	6.2

NONGRANULOMATOUS UVEITIS

Of the 16 patients with nongranulomatous uveitis associated with rheumatoid arthritis, there were five females (31 percent) and 11 males (69 percent), a reverse of the usual sex incidence of the disease. There were 15 white patients (94 percent) and one Negro (six percent). The arthritis preceded eye involvement in 11 or 69 percent of the patients with nongranulomatous uveitis, and in five patients (31 percent), the ocular inflammation preceded the articular symptoms. When the joint manifestations occurred first, they did so by an average of 10 years (with a range of one to 22 years). In the five patients (31 percent) in whom the eye manifestations occurred prior to joint involvement, the average precedence was 4.2 years, with a range of two months to seven years. In 12 cases (75 percent) the ocular disease was bilateral and in four (25 percent) it was unilateral. In the 16 patients with no granulomatous uveitis, the rheumatoid arthritis was inactive at the time of eye involvement in 12 (75 percent) and was active in four (25 percent). The visual acuity is of interest in this group: of the 16 patients, two had less than 20/200 in both eyes, eight had less than 20/200 in one eye, and eight had 20/50 or better in both eyes.

KERATITIS

The nine cases of proved corneal disease associated with rheumatoid arthritis were classified as in Table 3. As the cases of hypervitaminosis D and chrysosis corneae are due primarily to complications of therapy and not to the disease process per se, they are listed separately from the keratitides

TABLE 3

CORNEAL LESIONS IN RHEUMATOID ARTHRITIS

Keratitis sicca	2
Band keratopathy	2
Nodular keratitis	1
Chronic superficial keratitis	1
Hypervitaminosis D	2
Chrysosis corneae	1

more specifically associated with rheumatoid arthritis. Excluding these cases, all of the six instances of primary corneal disease were in females and all were white. The arthritis preceded the eye involvement in five of these. The disease was bilateral in five instances and unilateral in one. The average age of this group was 47, with an age range of seven to 70 years. Visual acuity was less than 20/200 in both eyes in one instance, less than 20/200 in one eye in two instances, and better than 20/50 in both eyes in two cases.

HYPERVITAMINOSIS D

An unexpected finding in this series was the occurrence of three cases of proven hypervitaminosis D. In two of these patients, the diagnosis was made by slitlamp detection of conjunctival and corneal calcification, while in the third, who had not received an ophthalmologic examination, the diagnosis was made at autopsy. The occurrence of hypervitaminosis D, however, is not surprising when one considers the chronicity of rheumatoid arthritis and the fact that large doses of vitamin D are often consumed by these unhappy patients for long periods of time.

The detection of these crystals in the cornea is of more than ophthalmologic interest, and suggest that all individuals with chronic rheumatoid arthritis who receive prolonged vitamin-D therapy should have periodic examinations of the eyes for the occurrence of these crystals. The early discovery of these crystals in such patients may be of life-saving importance. In the three instances here noted, one case was that of a 37-year-old woman with chronic Marie-Strumpell arthritis of 10 years' duration and no subjective eye symptoms; the second was a 65-year-old woman, with chronic polyarthritis since childhood, who had consumed 200,000 units of vitamin D daily for 18 months; the third was a 58-year-old woman, who died of chronic renal disease, and at autopsy findings were consistent with hypervitaminosis D.

CHRYSOSIS CORNEAE

Toxic reactions to gold therapy, such as dermatitis medicamentosa, aplastic anemia, and gold nephritis, were not infrequent in the total series. In this series, there was only one instance of classic chrysosis corneae, an incidence of 0.2 percent. The occurrence of this syndrome is a direct reflection of the intensity with which chrysotherapy is employed.

This patient was a 31-year-old woman, who developed an acute migratory polyarthritis 11 months prior to admission to the hospital. The disease had progressed until she was virtually incapacitated. Two months before admission, she was started on two injections of gold weekly. Within one week, she developed a stomatitis, and after three weeks had ocular pain with redness and photophobia. After receiving eight injections, the gold was stopped. Because the photophobia, pain, redness, and lacrimation persisted, she was referred to The Johns Hopkins Hospital.

Examination revealed that the vision in the right eye was 20/30−1 and in the left eye was 20/40. There was marked pericorneal injection, with tearing and blepharospasm. There was neither purulent conjunctival discharge nor preauricular lymphadenopathy. Slitlamp examination disclosed edematous conjunctivas, with both corneas showing numerous small subepithelial infiltrates at the limbus, and some deep brush-like vascularization of the corneal periphery. The aqueous flare was negative. There were no keratic precipitates, and the irises and lenses were normal. Ophthalmoscopy was negative in both eyes.

Because of the generalized gold reaction,

with urethritis and nephritis in addition to the bilateral marginal keratoconjunctivitis, she was started on BAL therapy. Considerable improvement occurred within one month, and, after two months, vision had risen to 20/15 in the right eye and to 20/20 in the left eye. Slitlamp examination then revealed a midstromal infiltration with irregular opacities in the peripheral millimeter of each cornea, with some fine superficial vascularization and a few deep vessels extending over the peripheral cornea, and the central portions of both corneas were clear. The final diagnosis was: (1) rheumatoid arthritis, moderate, subacute, involving shoulders, elbows, and toes; and (2) gold reaction, manifested by bilateral keratoconjunctivitis, urethritis, and nephritis.

Scleral involvement

One instance of scleromalacia perforans, which occurred as a late manifestation of rheumatoid arthritis, was noted in this series. This subject has been adequately covered in recent literature.[19] The chief finding of interest in this study is the infrequency of occurrence of either episcleritis or scleritis, and these likewise were late complications of chronic rheumatoid arthritis.

Incidental ocular findings

The various other unrelated major ocular disturbances encountered in this group of 465 patients, and confirmed by ophthalmologic consultation, are shown in Table 4.

TABLE 4

INCIDENTAL OCULAR FINDINGS IN 465 CASES OF RHEUMATOID ARTHRITIS

Branch vein thrombosis	2
Myopic posterior staphyloma	1
Retinal detachment, bilateral	2
Corneal opacities, marginal	1
Chorioretinitis, inactive	3
Retinal hemorrhages, secondary to gold aplastic anemia	1
Episcleritis (history of)	2
Fuchs' dystrophy	1
Cataracts, senile	2
Glaucoma	2
Macular degeneration	2

Vail[8] noted that choroiditis and retinal detachments have been reported in association with various joint diseases, and has emphasized that in Still's disease cases of bilateral retinal detachment with spontaneous cure have been seen. Evidence of posterior uveal involvement was conspicuous by its rarity in this series of rheumatoid arthritis patients. One patient with nongranulomatous iritis had an associated recurrent macular edema, but this was the only instance of active posterior segment inflammation in the total series. The cases of inactive chorioretinitis were instances of old, healed foci of granulomatous disease, and appeared unrelated to the arthritis.

Although not tabulated specifically, minor findings (conjunctival hyperemia or pallor, chronic blepharitis, and conjunctivitis) were occasionally described in the medical histories.

Distribution of ocular lesions in subgroups of rheumatoid arthritis

The occurrence of ocular lesions in four clinically recognized variants of rheumatoid arthritis is shown in Table 5.

TABLE 5

SUBGROUPS OF RHEUMATOID ARTHRITIS: OCULAR COMPLICATIONS

	No. Cases	% Total Group	Uveitis	% Subgroup	Keratitis	% Subgroup
Marie-Strumpell	27	(6.0)	4	(15.0)	1 (hypervitaminosis D)	3.7
Psoriatic arthritis	13	(2.8)	1	(8.0)	0	0.0
Felty's syndrome	7	(1.5)	1	(14.0)	1 (keratitis sicca)	14.0
Still's disease	14	(3.0)	1	(7.0)	1	7.0

Fig. 1 (Smith). Nodular keratopathy in Still's disease.

Marie-Strumpell disease

Of the 27 cases of Marie-Strumpell arthritis, 22 were males (82 percent) and five were females (18 percent). Four cases, one fourth of the entire number with nongranulomatous uveitis, occurred in this group, an incidence of 15 percent. One patient with Marie-Strumpell arthritis had ocular manifestations of hypervitaminosis D.

Psoriatic arthritis

It has been stated that psoriasis occurs in approximately three percent of patients with rheumatoid arthritis, and in only 0.7 percent of a comparable control group.[19] Thirteen patients (three percent) in this series of 465 patients with rheumatoid arthritis had concomitant chronic generalized psoriasis. One of these had nongranulomatous iritis, and one had an old healed chorioretinitis of undetermined etiology. It is of interest that Vail,[8] in 1951, predicted that nongranulomatous iritis should be found in psoriatic arthritis, but pointed out that no cases had been reported to that date.

Felty's syndrome

Seven patients fulfilled the clinical criteria of Felty's syndrome (rheumatoid arthritis, leukopenia, splenomegaly, and pigmentation). One of these had both keratitis sicca and nongranulomatous uveitis.

Still's disease

There were 14 patients with Still's disease, or juvenile rheumatoid arthritis. They were equally divided as to sex. The average age of these patients was 6.7 years. In one of these patients, the ocular lesion was the presenting complaint, an amazing case of nodular keratopathy, which improved dramatically on adrenocorticotrophic hormone therapy on two repeated occasions (fig. 1). One other patient in this group had a nongranulomatous iritis.

Discussion

The ophthalmologic literature is in need of clarification concerning the ill-defined

term, rheumatic iritis, so widely employed in the older literature. This term has been indiscriminately applied to any anterior uveal lesion which may occur concomitantly with inflammatory joint disease of any type—whether it be rheumatoid arthritis, gonococcal arthritis, disseminated lupus erythematosus, or even such entities as Behcet's disease, Reiter's syndrome, or Stevens-Johnson syndrome—where the etiologic agents range from bacterial and viral infections to presumed allergic reactions. The truth is that if iritis is present, it speaks against the diagnosis of rheumatic fever and for the diagnosis of rheumatoid arthritis.

With regard to chrysosis, Zavalia and Oliva[20] in 1939, reported an interesting study of 50 patients whom they treated with gold salts and followed from the beginning of therapy until several months following termination of treatment. After the administration of one to two gm. of Sanocrysin, subepithelial crystals, appearing as ultrafine granules on Bowman's membrane, were noted. These were present for the most part in the central cornea and decreased toward the periphery. This deposition of gold crystals was progressive and reached its maximum after approximately four gm. of Sanocrysin had been given, but did not increase further. At the height of the process, gold granules began to infiltrate the deeper corneal layers. This infiltration started peripherally and was thickest there. As it progressed to the center it became thinner and involved only the deep layer in the region of Descemet's membrane. One to two months after gold therapy had been stopped, the superficial crystalline deposits regressed and ultimately disappeared in all cases. The deeper infiltrations, however, remained and were observed as long as 12 years after therapy. These authors suggested that the superficial deposits were Sanocrysin crystals and the deeper dustlike bodies were particles of colloidal gold or some other gold salt.

Duke-Elder[21] lists nine ocular changes associated with rheumatoid arthritis; that is, chronic hyperemic conjunctivitis, chronic blepharitis, episcleritis, scleritis, sclerotenonitis, iritis, choroiditis, band keratopathy, and scleromalacia perforans. These lesions tend to localize in the collagen tissues of the eye. It is interesting that the corneal epithelium derived from surface ectoderm is characteristically uninvolved until late in band keratopathy, whereas the stroma, of mesenchymal origin, is the site of initial calcium crystal deposition. As data accumulate with regard to the pathophysiology of rheumatoid arthritis and especially its fascinating ocular manifestations, the basic mechanisms of this disease may well provide an important background for the understanding of other significant ophthalmologic disease entities.

It is suggested that every patient undergoing a survey for nongranulomatous uveitis have roentgenograms of the sacroiliac joints. The earliest X-ray changes of Marie-Strumpell arthritis, with its 15 percent incidence of iritis in this series, may thus be found. The often quoted comment that any patient having difficulty placing his chin in the slitlamp apparatus should be suspected of Marie-Strumpell arthritis bears repetition. All patients with rheumatoid arthritis receiving either vitamin-D or gold therapy should have careful biomicroscopic search for corneal and conjunctival manifestations of hypervitaminosis D as well as chrysosis corneae. The visual prognosis in a very small series appears poorer in patients with rheumatoid arthritis having corneal involvement than those with uveal tract disease. Finally, the medical profession should be alerted to the necessity for referring patients with rheumatoid arthritis promptly for ophthalmologic consultation because of the known propensity for eye involvement in this disease.

Summary

A review of the ocular lesions occurring in 200 cases of rheumatic fever and 465 cases of rheumatoid arthritis seen in The Johns

Hopkins Hospital between 1946 and 1952 has been presented. No instance of nongranulomatous uveitis was encountered in the 200 cases of rheumatic fever. Twenty-nine cases of associated ocular disease, including 16 cases of nongranulomatous uveitis, were found among the 77 patients with rheumatoid arthritis referred for ophthalmologic consultation. The over-all incidence of ocular complications in rheumatoid arthritis was 6.2 percent, and the incidence of nongranulomatous uveitis was 3.7 percent. The occurrence of ocular complications in association with Still's disease, Felty's syndrome, Marie-Strumpell arthritis, and psoriatic arthritis has been considered.

The Johns Hopkins Hospital (5).

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Ophthalmic Miniature

A young mother, yet a slender girl, brought her wretched babe, and bade me spit upon the child's sore eyes; this ancient Semitic opinion and custom I have afterwards found wherever I came in Arabia.

G. M. Doughty, *Arabia Deserta*, 1921.

PULSELESS DISEASE (TAKAYASU'S DISEASE)*

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The first case report of pulseless disease was in 1908 by Takayasu.[2] Since that time there have been reports totaling approximately 100 cases, most of which have been reported in the Japanese literature. I was able to find only three reports in American ophthalmologic literature[1,3,4] even though the eye signs and symptoms are often what first causes the patient to seek medical advice. Because of the paucity of reports in the American ophthalmologic literature and because a case of this disease was recently seen at the Veterans Administration Hospital, Iowa City, Iowa, it was thought desirable to describe the syndrome and to add this case to the literature.

Pinkham,[3] in 1954, reviewed much of the world literature concerning pulseless disease.

Classical signs and symptoms

Classically pulseless disease consists of three cardinal signs. The most common sign and the one for which the disease is named is that of the absence of palpable arterial pulsation in the upper extremities, the carotid arteries, and the superficial temporal arteries. The second sign is that of arteriovenous anastamosis characteristically surrounding the optic nerve, as seen by ophthalmoscopy. The third cardinal sign is that of a hypersensitive carotid sinus which frequently results in attacks of syncope and vertigo.

Two additional signs often considered classical are those of the development of cataracts and the absence of a detectable blood pressure in the upper extremities. The development of cataracts usually occurs late (one to four years after the onset of the disease), and the cataracts may be either of the nuclear or of the complicated type. The nuclear cataract is the more common. The ocular signs are listed in Table 1; the generalized signs in Table 2. The ocular symptoms that may occur in pulseless disease are detailed in Table 3; the generalized symptoms in Table 4.

Typical fundus findings

One may find a normal appearing fundus early or possibly a few microaneurysms in the periphery of the retina. Later beadlike or rosarylike swellings are noted along the course of the veins. The later course may

TABLE 1

Ocular signs

Classical
Arteriovenous anastomoses located about the nervehead*
Development of cataracts (especially nuclear)*
General
Enophthalmos (slight)*
Dilatation of conjunctival and episcleral vessels
Cornea
Pigmented deposits located in Descemet's membrane
Krukenberg's spindles
Anterior uvea
Paralysis of accommodation (rare)
Mydriasis*
Unequal pupils
Atrophy of the iris*
Vascularization of the iris (occasional)
Retina
Pallor of the fundus
Obliteration of the peripheral arterioles of the retina
Very low blood pressure in the central retinal artery
Occasional picture of occlusion of the central retinal artery associated with primary optic atrophy
Cotton-wool exudates
Grayish white flecks located around the macula
Large retinal hemorrhages*
Tiny retinal hemorrhages (possibly microaneurysms)*
Dilated retinal vessels*
Spasm of retinal vessels and focal constriction
Retinal detachment*
Retinitis proliferans with vitreous hemorrhage

* Those most frequently seen.

* From the Department of Ophthalmology, College of Medicine, State University of Iowa.

TABLE 2

GENERALIZED (NONOCULAR) SIGNS

Classical
Absent palpable arterial pulsation in the upper extremities*
Hypersensitive carotid reflex*
Absence of detectable blood pressure in the upper extremities*
Central nervous system
Hemiplegia
Loss of memory
Episodes of speech disturbance (aphasia)
Delirium
Ear, nose and throat
Perforated nasal septum*
Ulceration of palate
Atrophy of facial muscles and facial bones
Enlarged thyroid
Skin and appendages
Delicate skin (whitish and transparent)
Fine and poorly pigmented hair
Loss of hair
Loss of luster of hair
Trunk and upper extremities
Arteriovenous aneurysms in tips of fingers
Clubbing of the fingers (unusual)
Pulsating subcutaneous arteries over the back, chest and upper abdomen
Lower extremities
Hypertension in legs*
Laboratory findings
Elevated sedimentation rate

* Those most frequently seen.

not be observed because of the development of cataracts but, if seen, there are large arteriovenous aneurysms located close to and encircling the nervehead. Very late in the disease the optic nerve shows primary atrophy, and it is covered by a wreath of arteriovenous aneurysms. The peripheral retina is atrophic with only a few vessels visible.

TABLE 3

OCULAR SYMPTOMS

Visual
Gradual or sudden loss of vision (permanent or transitory)*
Often occurs with elevation of the head
Flashes of light and other visual phenomenon
Field defects
Other
Attacks of pain in the eye and the orbit

* Those most frequently seen.

TABLE 4

GENERALIZED (NONOCULAR) SYMPTOMS

Central nervous system
Seizures*
Headache
Emotional instability
Upper extremities
Intermittent claudication
Coldness and paresthesias
Other
Pain in the jaw with mastication
Attacks of chest pain
Tachycardia
Amenorrhea and hypomenorrhea

* Those most frequently seen.

PATHOLOGIC PHYSIOLOGY

Pulseless disease is most frequently seen in young women. The disease occurs frequently during or after puberty and on the average about the age of 20 years.

An acute infection such as scarlet fever or tonsillitis may precede the onset of the disease.

Gradual occlusion of the aortic arch, innominate artery, left common carotid artery, and left subclavian arteries occurs and results in a decreased blood supply and hence impaired nutrition and anoxia to the head and upper extremities resulting in the signs and symptoms mentioned in Tables 1 to 4. The intracranial branches of the arteries are rarely involved, although occasionally the descending aorta may be involved. Ask and Upmark[6] believe that the ascending aorta and its branches are involved more frequently, possibly because the higher arterial pressure in these vessels makes them more prone to develop an allergic disorder.

The most frequent early symptom is that of recurrent transient blurring of vision occurring especially upon turning the face upward, or when quickly assuming an upright position. The blurring of vision is often associated with sensations of flashes of light. As the occlusion of the vessels progresses the visual symptoms occur more frequently and last longer. Frequently these patients hold their heads with their faces directed downward for they find the visual

acuity is often improved in this fashion. The improved visual acuity can often be correlated with an improved blood supply to the retina when the face is directed downward, for an increased blood supply can be seen by ophthalmoscopy when the face is turned downward as compared to the upright position.

As the gradual occlusion of the aortic arch and its branches continues, a collateral arterial system develops to help compensate for the diminished blood supply to the brain, the face, and the upper extremities. The ability of the collateral system, or the inability of the collateral system, to supply the nutritive material necessary to carry on the functions of the brain and the functions of the structures of the face and of the upper extremities helps to determine the absence of, or the presence of, the signs and symptoms mentioned in Tables 1 to 4 in patients suffering from this disease.

The collateral blood supply to the structures of the face is often sufficient to supply the necessary nutritive material for this area. The collateral blood supply is by way of the subclavian artery to the inferior thyroid artery, then to the thyroid gland and from here to the superior thyroid artery and then to the external carotid artery and to the vessels of the face. The collateral blood supply passing through the thyroid gland seemingly accounts for the enlarged thyroid in this condition.

The collateral blood supply to the brain is by way of the vertebral arteries of the circle of Willis, thence to the middle cerebral and to the anterior cerebral arteries. The blood supply to the brain is often insufficient and results in the hemiparesis, the loss of memory, and so forth, as mentioned in the tables.

The collateral blood supply to the vessels of the face and to the brain supplies small quantities of blood to the vessels of the eye. The amount of collateral supply to the eye is insufficient however and thus there results increasing anoxia and subnutrition to the eye and hence there occurs atrophy of the structures of the eye and especially of the retina.

The collateral blood supply to the upper extremities is by way of the pectoral branch of the thyrocervical trunk to the thoracodorsal artery, thence to the dorsal circumflex artery of the humerus and then to the profunda brachial artery. The collateral circulation to the upper extremities is usually sufficient to supply the necessary nutrition to this area.

Whenever there is a constant and markedly decreased arterial pressure such as occurs in the retinal arterioles the finer capillary channels are short circuited and arteriovenous anastomoses occur. The short circuiting of the capillary channels explains the early arteriovenous anastomoses seen in the periphery of the retina as well as the large arteriovenous anastomosis noted around the optic nervehead in the late stages of the disease. The clubbing of the fingers and the arteriovenous anastomosis seen in the tips of the fingers is explained in a similar manner.

Because of the decreased blood supply to the eye a lowered arterial pressure in the retinal arteries can be easily demonstrated by pressure on the globe. This finding of lowered arterial pressure in the retinal artery may be an early finding in this disease.

Gradual decrease in visual acuity may result from formation of cataracts presumably on the basis of decreased nutrition to the eye, or the decreased visual acuity may arise without cataract formation due to gradual atrophy of the peripheral retinal elements, which is also presumably on the basis of decreased nutrition to the eye.

Attacks of dizziness, convulsions, or unconsciousness seem to be associated with a hypersensitive carotid sinus and is often produced merely by the patient stretching his neck. These attacks can easily be reproduced by pressure on the carotid sinus. The hypersensitivity of the carotid sinus is explained on the basis of insufficient blood supply to this area over a long period of time. In addition there is an infiltration of the wall of the carotid sinus which causes a stiffness of

the wall and hence the flow of blood to this area is easily occluded which in turn calls forth the impulses from the carotid sinus receptors.

Etiology

There appear to be two definite groups of pulseless disease. One group is associated with pathologic findings compatible with syphilitic aortitis at post-mortem examination. The other group is more common in females and fits more closely the disease described by Takayasu.[2] In the latter group the pulseless syndrome is found to arise from thrombosis of the subclavian and carotid arteries. Biopsy of one of these arteries shows an arteritis affecting the adventitial and medial layers of the vessel coupled with a thrombosis in the lumen. The internal elastic membrane is disorganized. Histologically, Shimizu et al.[7] felt that the lesion was suggestive of a tuberculosis lesion and the presence of Langhans' giant cells was noted; however, no organisms were found by smear, guinea pig inoculation, or by culture.

Other theories have been advanced as the cause of the second group of cases and include Buerger's disease, allergy, panarteritis of unknown etiology, and collagen diseases.

Pathology

The pathologic findings in the major vessels involved is discussed above. Pinkham[8] and De Bes et al.[14] reported the pathologic findings in the eye and these included the findings noted in Table 5.

TABLE 5

Pathologic findings in the eye

Lens
Coagulation necrosis
Ciliary body
Atrophy of muscle and ciliary processes
Retina
Clumping of rods and cones
Ganglion cells decreased in number
New vessel formation in nerve-fiber layer
Central retinal artery
Marked proliferation of the intima
Optic nerve
Demyelinization

Laboratory findings

The principal laboratory findings are those of an elevated sedimentation rate, a leukocytosis, an increased prothrombin time, a positive tuberculin test,[7] and a positive serology in some cases.

Differential diagnosis

The principal diseases to include in the differential diagnosis are those of: temporal arteritis, Buerger's disease (thromboangiitis obliterans), and periarteritis nodosa.

Temporal arteritis is usually apparent in the superficial temporal arteries, and at times is a relatively benign and self-limited disease. The disease usually begins in people over the age of 55 years and has no predilection for the sexes. It is often associated with systemic symptoms of low-grade fever, generalized malaise, fatigue, night sweats, weight loss, and so forth. The disease tends to involve medium sized vessels—usually the cranial vessels—and most patients with temporal arteritis have symptoms of headache. Typically one often finds a hard tender cord, located in the temporal regions and representing the temporal arteries. The pathologic findings seem to simulate quite closely the findings in pulseless disease except that in temporal arteritis the adventitia is usually not as grossly affected.

Periarteritis nodosa occurs predominantly in males of the age group of 20 to 40 years. The disease tends to involve medium-sized arteries, especially those of the viscera, and tends to avoid the aorta. The symptoms are varied and numerous, although pain is quite frequent. Pathologically, periarteritis nodosa simulates pulseless disease in so far as the vessels are concerned except that there are no giant cells and in periarteritis there are often many eosinophils.

Buerger's disease is again a disease of the medium-sized vessels. This disease occurs predominantly in males in the age group of

20 to 45 years. The legs are usually principally affected and usually the disease is associated with severe pain. Pathologically, the vessels are involved in a panarteritis which is segmented leaving normal vessels between the involved segments.

Treatment

No known treatment is effective. Caccamise et al.[9] have suggested that Cortone or ACTH may be of value. Antiluetic treatment has helped in some of the cases which were found to have a positive serology. A thrombectomy performed through the external carotid artery and coupled with denervation of the carotid sinus and removal of the carotid body has been tried by Shimizu et al.,[7] with some relief of the symptoms. In another case Shimizu et al.[7] tried grafting a piece of vein into the area where the thrombosis had been resected. This relieved the attacks of syncope, but still there appeared to be little flow of blood to the brain through this segment. Sympathectomy of the cervical sympathetic ganglion has also been tried. If Shimizu and Sano[7] are correct in their postulate that tuberculosis is the etiologic factor it would seem that treatment with drugs active against this disease would be indicated, although they did not mention this possibility.

Prognosis

The prognosis is poor although some patients can carry on limited activity if their collateral circulation to the brain is sufficient. These people appear to be prematurely aged because of the central nervous system involvement.

The prognosis for vision is unfavorable. In a few cases cataract extraction has been performed only to reveal an atrophic retina. The end result is often that of light perception or complete blindness. The course of the disease is usually one and one-half to 14 years. Death results from chronic debility due to cerebral ischemia, although occasionally it may be the result of myocardial disease.

Case report

On July 3, 1954, J. H., a 47-year-old white man, was first admitted to the Veterans Hospital. His chief complaint was weakness of two to three years' duration, associated with a paralysis of the right side of two weeks' duration. In addition, the patient complained of symptoms compatible with intermittent claudication of two to three years' duration.

Family history was contributory only in that the patient was of Scandinavian extraction and that his father had pernicious anemia, and his mother had heart disease. In addition one brother had died of heart disease at the age of 47 years, while a second brother had had a heart attack three years before.

Initial examination revealed a blood pressure of 110/70? mm. Hg in the upper extremities. The pulse was difficult to obtain, although one observer thought he could palpate the pulse in the right radial artery. The pulses in the lower extremities could not be palpated. Neurologic examination was compatible with a right hemiparesis and hemianesthesia. At the initial examination the carotid arteries were readily palpable and a very loud murmer was audible over both carotids.

The patient was seen in the eye clinic for consultation on July 28, 1954, at which time the visual acuity was recorded as 20/20, O.U.; the fundus was normal; and the only unusual finding was that of arterial pulsation being obtained easily by slight pressure on the globes.

Laboratory findings revealed a negative serology, a sedimentation rate of 26 mm. in one hour. RBC: 4.2 million; HgB: 12.5 mg., and WBC: 9,600, with a normal differential. Urinalysis was normal. The fasting blood sugar was 95, and a glucose tolerance test was well within normal limits. The spinal fluid examination was normal.

X-ray studies of the chest and skull were read as normal. An electrocardiogram showed changes suggesting myocardial disease. Dicumarol therapy was started and con-

tinued for several weeks but was eventually discontinued when no improvement was noted.

The second hospital admission was on February 15, 1955, at which time the patient was admitted with a chief complaint of increased weakness of the right side and weakness and poor circulation in the left side and foot. The patient volunteered that he had had a second stroke in January, 1955. In addition, the patient complained of decreased visual acuity in the left eye, some speech difficulty, and increasing intermittent claudication. No pulses whatsoever were obtainable at this examination.

Oscillometric examination showed only slight excursion on the right upper extremity and slightly more in the left upper extremity. At this time the patient looked prematurely old.

The laboratory findings were similar to the first admission except that the WBC was now 14,400. Total protein was 7.6 (albumin 5.2; globulin 2.4). Total cholesterol 264 (esters 57 percent); PPD (1st strength, two plus). The electrocardiogram showed little change, being read as showing an incomplete right bundle branch block at this time.

Ophthalmologic examination revealed a visual acuity of 20/20, O.D., and 20/30, O.S. The fundus showed at this time many punctuate hemorrhages or microaneurysms in the far periphery associated with enlarged veins which had a segmented appearance. No lens changes were noted.

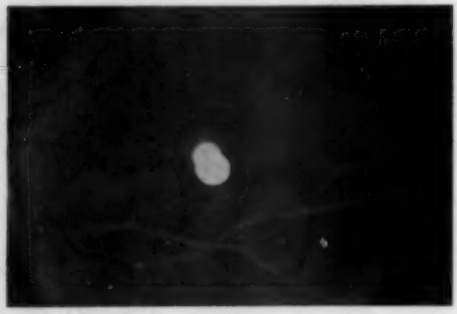

Fig. 1 (Ostler). Fundus changes in pulseless disease.

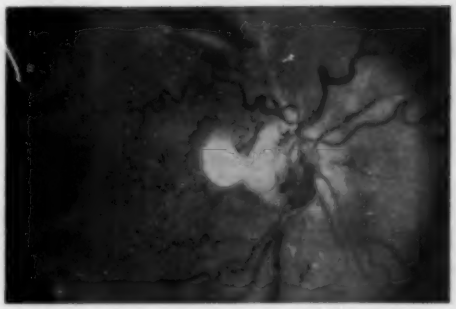

Fig. 2 (Ostler). Fundus changes in pulseless disease.

Examination late in November, 1955, revealed that the patient appeared at least several years older. Significant eye changes were found which included: visual acuity: O.D., 20/30; O.S., 20/40; beginning nuclear sclerosis, O.U.; and marked vascular changes in the fundus. The vascular changes in the fundus consisted of a silver wiring of several of the arterioles and increased tortuosity of most of the vessels, with rosary formations along the veins. Arteriovenous anastamosis occurred at the nasal side of the optic nerve and many flame-shaped and a few striate hemorrhages were present. Beginning proliferative retinopathy was noted in the inferior temporal quadrant of the left eye. Many of the changes noted in the fundus can be seen in Figures 1 and 2.

Biopsy of one of the involved vessels or arteriography was suggested to aid in the diagnosis but was thought to be inadvisable because of the precarious health of the patient.

The patient has not been seen by me since November, 1955. At that time he was confined to a wheelchair or to bed, for any slight exertion resulted in marked fatigue.

Summary

The classical and more common findings of pulseless disease are reviewed and a case is reported in which many characteristics of pulseless disease occurred in a 47-year-old white man of Scandinavian extraction.

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CEREBRAL ARTERIOVENOUS ANGIOMA*

An unusual cause of unilateral exophthalmos

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General information

The angiomatous malformations of the brain may be chiefly capillary (telangiectasia), chiefly venous (angioma venosum), or chiefly arteriovenous (angioma arteriole, arteriovenous aneurysm) in their composition.

The telangiectasia, including the syndrome of Sturge-Weber, are malformations of the capillaries or precapillary blood vessels, and are well-defined anatomic and clinical entities. They will not be considered in this report.

The true venous angiomas are rare, for in these cases both the feeding and draining vessels must be veins. However, a few authentic cases of this variety of angioma have been described in the literature. As pointed out by Cushing and Bailey,[1] most venous angiomas are closely related to arteriovenous angiomas and may, anatomically, be indistinguishable from them. Olivercrona[2] feels that the difference between a venous and an arteriovenous angioma is a physiologic one and depends on the extent of the arterial blood supply. He likewise feels that most cases described in the literature, as instances of venous angioma, are in all probability examples of true arteriovenous angioma.

In the true arterial angioma, both the feeding and draining vessels must theoretically be arteries or have a histologic structure resembling arteries. According to Olivercrona,[2] such a lesion might exist but no convincing case has as yet been published. Among the cases described in the literature under this heading, in which the available facts are sufficient for the formation of an independent opinion, the draining vessels

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have always proved to have the anatomic character of veins. Probably all the arterial angiomas described in the literature under this name are, in reality, arteriovenous angioma.

Thus by excluding the telangiectasia and Sturge-Weber disease, we find that, while arterial and venous angiomas can occur, the arteriovenous angiomas are by far the most common and, clinically, the most important cerebral vascular malformation of this group.

In the true arteriovenous angioma, the arterial blood enters directly into a vein since the capillary net belonging to the artery is missing. This capillary net has been replaced by a tangle of abnormal blood vessels interpolated between the artery and vein. The veins draining the tangle of blood vessels are dilated and pulsating and contain arterial blood. The feeding arteries are hypertrophied and dilated.

Development

These malformations are thought to be congenital and are undoubtedly attributable to some fault of development.

According to Cushing[1] and Bailey, the development of the blood supply of the brain has been divided by Streeter[3] into five periods. In the first period, the primordial vascular plexus is established. In the second period, this plexus resolves itself into arteries, veins, and capillaries.

The third period is characterized by a splitting of the vascular system into three superimposed layers by the development of the dura mater and cranium, so that a superficial, a dural, and a pial circulation results.

The fourth period produces a series of changes in the arrangement of the vascular trunks and finally, during the fifth period, the late histologic changes occur, resulting in the structure of adult arteries and veins. It is possible that a maldevelopment of a vascular area during the third period might result in the association of a vascular nevus of the scalp and varices of the dura, of varices of the dura and a venous angioma of the pia, or of all three simultaneously.

Pathology

A. Arterial angioma

Arterial angioma refers to a vascular tumor consisting exclusively of a conglomeration of coiled arteries. Since the title, arterial angioma, has often been employed for lesions containing veins as well as arteries, most of the cases reported in the literature are in reality cases of arteriovenous angioma. To establish the diagnosis of a purely arterial angioma, both the afferent and efferent vessels, as well as those vessels actually comprising the tumor, must all have an arterial structure. Using this as a criterion, it is doubtful whether such a lesion can be found.

B. Venous angioma

The classic variety of venous angioma[4] is a wedge-shaped or cone-shaped lesion in which the base of the cone is in contact with the leptomeninges and the tip reaches the ventricle. An aggregation of intertwining vessels is usually observed on the surface overlying the involved area. Within the brain there is a tangled mass of large vessels which are separated from each other by thin layers of cerebral tissue, the resultant appearance somewhat resembling a variocele. The lesion may actually protrude into a ventricle and, if large enough, may actually fill the ventricle, thereby giving rise to an obstructive hydrocephalus.

Venous angioma is not an expansive tumor but rather it replaces the tissue of the involved area and not uncommonly causes a definitive atrophy of the region, which may be evidenced by considerable dilatation of the nearby ventricle and a pool of fluid overlying the shrunken cortex.

Not infrequently some bleeding results from the tumor, which is commonly evidenced by a thin layer of subarachnoid

blood. Larger hemorrhages may also occur either intracerebrally or into the ventricles. Areas of encephalomalacia are to be found adjacent to the tumor.

Microscopically most of the vessels in a venous angioma resemble the structure of normal veins. The vessels are usually irregular and bizarre in shape. Their walls are relatively thin but may show considerable variation. The cerebral parenchyma separating the vessels and surrounding the lesion manifests rather marked changes such as demyelination, degenerative changes in the nerve cells, gliosis, encephalomalacia, and occasionally hemorrhages.

C. Arteriovenous angioma

1. *Gross pathology.* Arteriovenous angioma[4] occurs most commonly in the cerebral hemispheres and only rarely in the cerebellum. The angioma often occurs as a wedge-shaped lesion extending deep into the brain parenchyma. Usually the entire surface of the involved region is covered with a dense plexus of angiomatous vessels (fig. 1). Not infrequently large abnormal vessels are observed over extensive areas of the brain surface not related to the principal vascular tumor. These vessels, as well as those overlying the angioma itself, often connect with enlarged tortuous vessels situated over the basilar structures. The latter vessels in rare cases may course along the optic nerve to reach the orbit. A moderate degree of dilatation and hypertrophy of the artery supplying the region involved by the angioma frequently occurs. Some portion of the angioma is usually in contact with one of the ventricles, occasionally producing considerable compression and even obstruction of the involved portion of the ventricle.

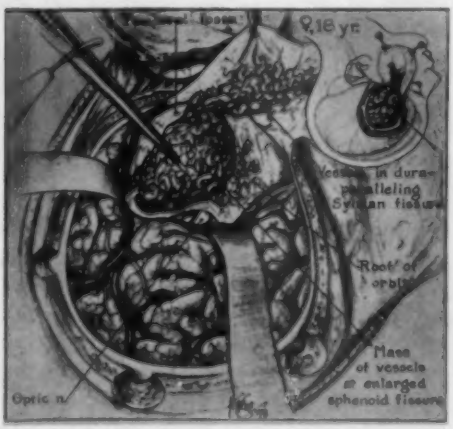

Fig. 1 (Alfano and Reese). Tangle of angiomatous vessels on surface of cerebral cortex in a case of arteriovenous angioma (after Walsh[9]).

Microscopically, this variety of angioma is comprised of a collection of adult blood vessels which are separated from one another by brain tissue. The general histologic picture is similar to that described for venous angioma; however, scattered throughout an arteriovenous angioma are numerous vessels clearly resembling arteries.

These arteries tend to be round or oval but may be irregular in contour. Their walls are generally thick, with the individual vessels revealing little variation in their mural thickness. Degenerative changes in the vessel wall are not prominent, but calcification of scattered vessels is the rule. The parenchyma surrounding the lesions, and separating the individual vessels, shows considerable degenerative changes, such as disease of nerve cells, demyelination, encephalomalacia, and gliosis. Extensive hemorrhages and large cerebral softenings are not uncommon.

Secondary changes may occur in these arteriovenous angiomas and the most frequent and clinically important of these is hemorrhage. It is estimated that this change may occur in as high as 50 percent of the cases. Repeated hemorrhages can also occur. In most cases the hemorrhage is both subarachnoid and intracerebral.

Thrombosis is comparatively rare and, when it does occur, takes place gradually and without obvious clinical symptoms. The

only indication of thrombosis is calcification, which appears as round shadows, representing cross-sections of larger blood vessels, probably veins draining the angioma.

Frequency

Arteriovenous angiomas of the brain are comparatively rare lesions. According to Dandy[3] they occur in about one percent of a series of brain tumors. Sixty cases of arteriovenous angioma were observed in a series of 3,026 cases of verified brain tumors, reported by Olivercrona,[2] who felt that with the introduction, frequent use, and perfection of arteriography, an increase in the diagnosis of arteriovenous angiomas could be expected.

Sex and age incidence

These angiomas[1] occur with much greater frequency in males than in females, the ratio being about 2:1.

Since these angiomas are congenital malformations, the first symptoms might be expected to occur at an early age. This, however, is not the case, and the appearance of symptoms before the age of 10 years is comparatively rare. The majority of patients have their symptoms during the second and third decade of life, although cases have been reported as occurring as early as the age of two and one-half years.

The reason that a lesion present at birth does not, in the majority of cases, give rise to symptoms until decades later is not known. To some extent this may be explained by the undoubted progressive nature of the arteriovenous angioma; the lesion being comparatively small at birth and only gradually attaining a size capable of affecting the circulation of blood in the brain sufficiently to give rise to symptoms. Another fact to be considered in this connection is the occurrence of secondary changes in the lesion such as rupture of blood vessels and thrombosis, which may conceivably require some time to develop.

General symptoms and signs

The cardinal signs are epileptic fits, subarachnoid hemorrhages, and usually a hemiplegia.[1,6] Other signs are less common but may occasionally, in combination with one or more of the preceding symptoms, be pathognomonic, particularly a systolic bruit or a calcification of typical appearance.

The first symptoms usually occur at a comparatively early age, in the majority of cases during the second or third decade of life. It is rather characteristic that the symptoms at first occur at long intervals, during which the patient has good health, until years later the initial symptom recurs or a new one appears. Gradually as the illness progresses, a tendency to increasing frequency and intensity of symptoms is described.

Headache[1] is a frequent complaint but is usually not characteristic. Occasionally, however, attacks of headache closely simulating migraine can occur, particularly if the angioma is located in the region of the occipital lobe or parieto-occipital area.

Since the majority of patients having headache show no signs of an increased intracranial pressure some other explanation for the occurrence of headaches must be sought. Olivercrona[2] feels that anoxemia of the brain due to shunting of the blood through the abnormal arteriovenous communication is the most likely cause. Anoxemia of the brain results in dilatation of cerebral vessels, which is known to be painful.

A systolic bruit[1,2,6] may be present but is not a frequent finding. It is of almost pathognomonic significance, although a bruit may also be heard with carotid artery-cavernous sinus fistula and occasionally with unruptured saccular aneurysms or with very vascular meningiomas. Increased vascularity of the scalp and bony cranial structures is sometimes observed even in comparatively early cases.

In addition to the increased vascularity, the entire vascular system of the head may

be enlarged and on surgical exposure one may find a definite enlargement of the common and internal carotid arteries.[1,2,6] Small angiomas may be present on the skin of the face or the scalp.

Mental changes occur[1,6] in about 50 percent of these patients, particularly those of long standing.

The angiograms are pathognomonic and show several huge tortuous arteries leading to a dense tangle of vessels from which several veins emerge.[6] In anteriovenous anomalies, the cerebral circulation has a greater velocity than normal because of the enlarged vascular bed and the presence of many wide, direct arteriovenous communications. One, therefore, sees simultaneous filling of arteries and veins during the arterial phase of the angiogram.[6]

Encephalograms may reveal either a local or general cortical atrophy.[1,6]

Ocular signs and symptoms

Although the vision in the cases surveyed is usually recorded as normal, unilateral as well as bilateral visual loss has been reported.[1,2,6,7] Engorgement and dilatation of the conjunctival and episcleral vessels may occur. Dilatation of the ipsilateral pupil was reported by Turner[7] and Jaeger.[8] Diplopia without the actual demonstration of an ocular muscle paresis has been known to occur.[7,8] Diplopia associated with a paresis of the ipsilateral lateral rectus is more likely to be present.[2]

Exophthalmos[2,7,8] has been reported, although it does not appear to be a common occurrence. The exophthalmos is usually unilateral and is then always on the side of the lesion. Bilateral exophthalmos may be present, and in these cases the exophthalmos is greatest on the same side as the lesion. Occasionally, the exophthalmos is pulsating; the clinical picture then resembling the variety of pulsating exophthalmos due to a carotid artery-cavernous sinus fistula from which condition arteriovenous angioma must be differentiated. Walsh[9] reported a case of intermittent exophthalmos due to an arteriovenous angioma in the region of the superior orbital fissure. He feels that in the absence of a pulsation in these cases, the malformation is probably of a venous nature.

Diminished corneal sensation was present in one case reported by Dandy.[5]

In the earlier literature[1] the occurrence of a choked disc was said to be a frequent symptom. However, in the later literature[7,8] choked disc as well as the other signs of an increased intracranial pressure are frequently lacking. Cushing[1] felt that while the venous angiomas were most apt to be unaccompanied by a choked disc, the arteriovenous angiomas were more apt to be and exophthalmos was more frequent in the latter type.

Increased vascularity of the eyegrounds, with dilatation and tortuosity of the retinal vessels has been described by various authors.[2,5-8] In about 20 percent of the cases an increased vascularity of the skull may be evident upon radiologic examination.[6]

Defects in the visual fields appear not to be common although homonymous sector and hemianopic defects have been reported by Cushing,[1] Turner,[7] and Jaeger.[8]

Treatment of this condition has varied from time to time and has included ligature of the feeding arteries, ligature of the internal or common carotid artery, roentgen therapy, decompression for the relief of papilledema, and excision or coagulation of the lesion.

Olivercrona[2] feels that the choice lies between surgically removing the lesion or leaving it alone. In case of the latter, roentgen therapy may be tried, even if not much is to be expected from such therapy.

Differential diagnosis

Although this condition must be differentiated from all those conditions which are known to produce exophthalmos, it must in

particular be differentiated from a hemangioma of the orbit and a carotid artery-cavernous sinus fistula.

Hemangiomas usually arise from the muscle cone and hence produce an axial exophthalmos. There may be an associated engorgement of the veins of the lids, conjunctiva, and sclera, as well as subconjunctival hemorrhages. A paresis of the external rectus muscle may be in evidence. On rare occasions the exophthalmos may pulsate but there is never a bruit. Roentgenograms of the orbit may reveal an increased soft tissue density but calcifications are extremely rare. Arteriograms reveal a normal cerebral circulation.

Carotid artery-cavernous sinus fistula may be traumatic or spontaneous, and usually gives rise to a pulsating exophthalmos. The exophthalmos in these cases is usually quite marked, the eye being most frequently deviated down and out. The exophthalmos is often unilateral but frequently becomes bilateral. There is marked edema of the lids of the proptotic eye, as well as chemosis of the conjunctiva which may be of sufficient degree to protrude through the palpebral aperture. There is usually dilatation of the veins of the skin, particularly the superior orbital, as well as the veins of the conjunctiva and sclera.

The exophthalmos is pulsating and frequently accompanied by a bruit which is usually best heard over the globe or the ipsilateral orbit or side of the head. The bruit can be obliterated or at least reduced in intensity by compression of the ipsilateral carotid artery in the neck. There may be an associated paresis of the third, fourth, and sixth nerves.

The fundi usually reveal some venous distention and, occasionally, retinal hemorrhage. Edema of the nervehead may be present. A secondary glaucoma due to an increased venous pressure may supervene.

Skull X-ray studies in the traumatic variety may reveal, but frequently do not, a fracture of the body of the sphenoid bone. In the spontaneous variety, skull X-ray films may reveal deposition of calcium in the wall of the ruptured aneurysm. Arteriograms usually reveal passage of the dye directly from the internal carotid artery into the cavernous sinus and from there into a dilated and tortuous superior ophthalmic vein.

Case report

The patient was a 67-year-old, white woman whose history dates back to September, 1952, at which time she had experienced a peculiar intermittent snapping sensation in her right ear associated with a proptosis of the right eye which persisted for about 20 minutes. In December, 1952, she had a recurrence of the same symptoms which subsided spontaneously and without treatment. In March, 1953, she again experienced a sudden proptosis of the right eye, with diplopia and pain over the right temple. Since her symptoms of proptosis and diplopia failed to subside after a period of six weeks, she presented herself to the eye clinic for examination.

Systemic examination was noncontributory. Blood pressure was recorded as 130/80 mm. Hg. There were three small angiomas in the center of the forehead and one in the center of the right upper lid (fig. 2). The right supraorbital vein was dilated. Visual acuity with correction was 20/20 in each eye.

Eye examination. The right eye revealed in addition to the angioma of the right upper

Fig. 2 (Alfano and Reese). Although taken after postcarotid ligation, this shows the prominence of the right eye and the angioma of the forehead and right upper lid.

Fig. 3 (Alfano and Reese). Although taken postoperatively, this shows prominence of right eye with slight residual right esotropia. Note residual dilatation of episcleral vessels in conjunctiva over temporal one half of globe and conjunctival angioma in region of medial canthus.

Fig. 4 (Alfano and Reese). Although taken postoperatively, this still shows some remaining paresis of right external rectus. Conjunctival angioma in medial canthus now more obvious.

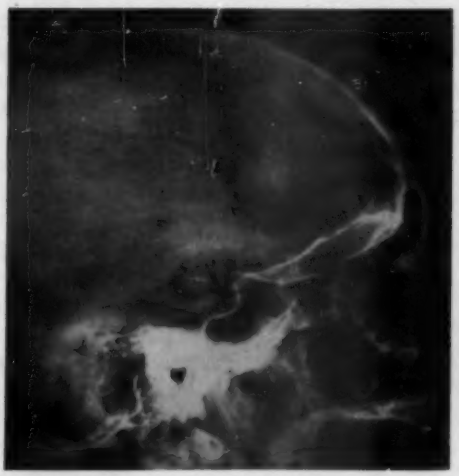

Fig. 5 (Alfano and Reese). Roentgenogram of skull showing parasellar calcification.

lid a moderate edema of the upper and lower lids and the conjunctiva (fig. 3). There was a small conjunctival angioma in the region of the medial canthus (fig. 4) and a conjunctival hemorrhage over the area of insertion of the external rectus muscle.

The eye was exophthalmic (fig. 4), measuring 27 mm. as compared to 17 mm. for the left eye. The exophthalmos was nonpulsating and nonreducible. No bruit was discernible. Pupillary reaction was normal.

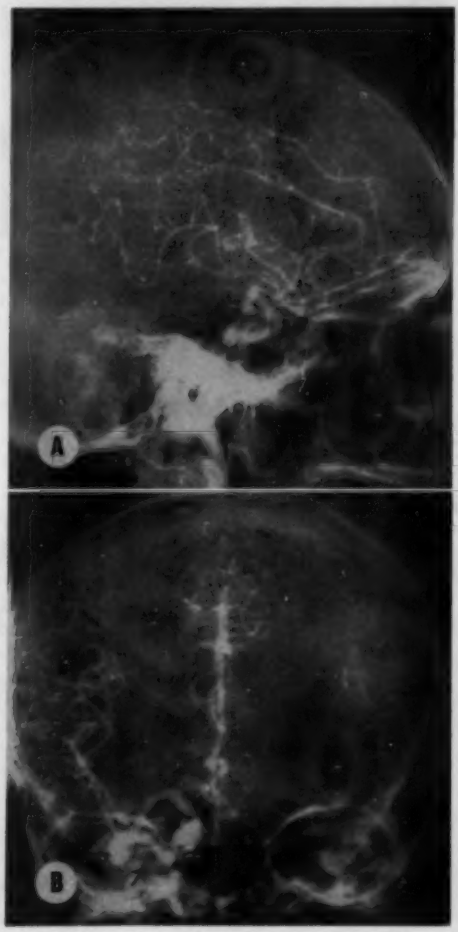

Fig. 6 (Alfano and Reese). (A) Right internal carotid artery angiogram (lateral view) showing angioma (single arrow) and dilated superior ophthalmic vein (double arrow). (B) Anteroposterior view.

Fig. 7 (Alfano and Reese). Right internal carotid artery angiogram. Anteroposterior view, showing calcification (arrow) in right internal carotid artery.

External examination of the left eye was normal. Ocular muscle balance revealed an esotropia (fig. 3) of the right eye on the basis of a right external rectus paresis (fig. 4).

Fundus examination. The right fundus revealed a normal disc with dilated and tortuous veins. No hemorrhages were present. The left fundus was considered as being normal. Roentgenologic examination of the orbits revealed an increased soft tissue density on the right side. Skull X-ray films were considered normal except for a parasellar calcification on the right side (figs. 5 and 7). Carotid arteriogram (fig. 6-A and B) revealed an arteriovenous angiomatous communication between the internal carotid artery and superior ophthalmic vein at the level of the posterior clinoid process.

A ligation of the right internal carotid was performed following which the edema of the lids and conjunctiva disappeared, as did the engorgement of the episcleral veins. However, the exophthalmos remained the same at the time of her most recent examination six months after carotid ligation. The paretic right external rectus had improved but complete return of function was not present, although the patient was no longer troubled with diplopia. Tonography performed on both eyes postoperatively was considered as being normal.

Conclusion

A case of unilateral exophthalmos has been presented which resulted from an arteriovenous angiomatous communication between the internal carotid artery and the superior ophthalmic vein at the level of the posterior clinoid process in a patient who, in addition, showed an angioma of the forehead, ipsilateral upper lid, and conjunctiva. This condition, should be considered in the differential diagnosis of all cases of unilateral exophthalmos.

The classical picture consists of epilepsy, signs of subarachnoid hemorrhage and intracerebral hemorrhage, and hemiplegia in an individual who may show angioma of the skin. Diagnosis can usually be confirmed by skull films which may show typical calcifications and an increased vascularity of the bones of the skull. The lesion is usually revealed by arteriography.

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RELATIONSHIP OF PLEUROPNEUMONIALIKE ORGANISMS AND UVEITIS*

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The organisms of the pleuropneumonialike group have as yet not been reported in ophthalmic literature to be associated with iritis. There are reasons to believe, however, that such a relationship does exist and in certain cases may be of etiologic significance. Inasmuch as this area of ophthalmology has not been previously presented, a rather complete historical survey of this unique group of organisms seems advisable in conjunction with the clinical material.

BACTERIOLOGIC ASPECTS

The pleuropneumonialike organisms themselves are indeed of peculiar interest in that they occupy a position intermediate between viruses and bacteria. Particle sizes still capable of multiplication as determined by ultrafiltration and electron micrographs vary between 170 and 250 millimicrons[1] which is about the same particle range exhibited by the viruses of molluscum contagiosum and vaccinia. Sabin[2] established definite criteria required of organisms included in the group. They differ from viruses in that they are cultured on lifeless media. Were this not true they would undoubtedly be classified with the viruses.

Cultural media required by the organisms of the pleuropneumonia groups must include a lipoprotein containing only bound cholesterol and phospholipid[3,4] which is usually supplied by 25-percent ascitic fluid or 10-percent horse serum in broth or agar. On solid media the pleomorphic character of these organisms is revealed including "rings," filaments, globules, and minute filterable elemental bodies which are the reproductive units. The colonies vary between 10 and 300 microns in diameter but may be as large as 600 microns, extending into the agar in the central area. Usually, magnification is required for study. Identity of the organisms is suggested by gross appearance of the colony but staining by the method of Dienes[3] is of greatest value to reveal the typical spongelike character with minute coccoid and bacilliform bodies at the periphery. The normal bacterial growth cycle is followed, as determined by turbidimetric and viability counts.[4]

"L" PHASE ORGANISMS

Thus far in this presentation the "L" forms have not been mentioned. Essentially these are bacterial variants or products of bacterial de-differentiation having almost identical cultural characteristics and appearance to those of the pleuropneumonialike group. When repeatedly subcultured, especially in penicillin-free liquid or semisolid media, they tend to revert back to the parent organism in some instances. Such "L" cultures have been isolated from bacterial cultures of Clostridia, Proteus, H. influenzae, Salmonellae, Bacteroides, and others, frequently with the aid of penicillin added to

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the media. In some cases the "L" phase organisms have been obtained from patients' bronchial tree while the patients were under penicillin therapy.[6]

Some workers claim to be able to distinguish the "L" forms from pleuropneumonialike organisms on the basis of morphology and growth rate at the time of initial isolation. Cholesterol or other sterols do not appear to be required for the growth of the "L"-phase, as is required for the pleuropneumonialike organisms.[6]

Of 91 strains of pleuropneumonialike organisms isolated from the human genital tract all except one were similar.[7] Similar carbohydrate fermentations were obtained with strains of these organisms; hence, close relation to one another is suggested. Since the "L"-phase variant has been observed to ferment the same carbohydrates as did its bacillary ancestor[8] the pleuropneumonialike organisms as a distinct group seems certain.

Through the inoculation of pleuropneumonialike organisms into rabbits, antibodies are formed which can be demonstrated by neutralization of pathogenic strains in culture, and by agglutin, precipitin, and complement fixation reactions.[6] However, from these studies there appear to be many antigenic strains, attesting to the heterogeneity of the group. From the evidence at hand there does seem to be good reason to consider the pleuropneumonialike organisms as a group distinct from the "L"-phase organisms. In this study no attempt was made to differentiate pleuropneumonialike organisms from "L"-phase organisms.

Occurrence in nature

The pleuropneumonialike organisms have been known since 1898 when Nocard, et al.[9] isolated the etiologic agent of a highly contagious pleuropneumonia of cattle. Then, in 1923, Bridré and Donatien[10] found a pleuropneumonialike organism in goats and sheep suffering from agalactia, a syndrome of keratitis, arthritis, skin lesions, and mastitis, with suppression of lactation. The organism was isolated from the conjunctival sac, milk, joint fluid, and blood stream.

In mice certain *endogenous* strains of pleuropneumonialike organisms, which are often present in the absence of disease, have been shown to produce a conjunctivitis as well as polyarthritis, infectious catarrh, and neurologic disease.[6] If these organisms are given intravenously to a young mouse "rolling disease" due to cerebellar infection develops, but if older, more resistant mice are inoculated in the same manner a type of polyarthritis develops with migratory, fusiform joint swellings from which positive cultures for pleuropneumonialike organisms can be obtained for over two months even though the blood is negative in two or three days. This arthritis responds to therapy with gold salts in much the same manner as do some human cases.[3] Several different mouse strains have been isolated but human strains are not pathogenic for mice or any other known laboratory animal.

Hence, it is well known that pleuropneumonialike organisms do cause disease even though they may be present in certain tissues of normal animals.

Human incidence

In 1937 Dienes and Edsall[11] isolated pleuropneumonialike organisms from a laboratory worker with an abscess of Bartholin's gland. This is the first recorded isolation of the organism from a human. Since that time isolations from different parts of the human body have been made by numerous observers. They have been found in saliva in 46 percent of 100 normal subjects and in 33.6 percent of 144 normal throats.[12] There was no sex difference in incidence and no correlation with oral lactobacillus counts. Certain strains of the oral organisms appear to differ serologically and on culture from those of genital origin.

It cannot be ignored that organisms of the

pleuropneumonia group have been found, frequently in pure culture from severe human infections aside from those of the genital tract, even though absolute proof of their etiologic significance is lacking. In three instances of purpura, blood cultures for these organisms were repeatedly positive.[13,14] Blood cultures have also been reported to be positive for pleuropneumonialike organisms in a case of human bite, postpartum septicemia,[15,16] and a case of subacute bacterial endocarditis[17] as well as a posttraumatic brain abscess.[18] This abscess resulted from a pipe stem perforating the orbit between the medial rectus and medial orbital wall to enter the frontal lobe of the brain through the superior orbital fissure. Since the organism has never been reported in the conjunctiva, the assumption is that this organism was an oral strain introduced on the pipe stem. Also, the pleuropneumonialike organisms have been grown in almost pure culture from an empyema of the chest following lung resection for bronchiectasis.[18]

Genital isolation of the pleuropneumonialike organisms has formed the major area of investigation in the human occurrence of these organisms. Dienes, et al.[3] found the organisms in 26 percent of 222 normal females, while Salaman[19] found pleuropneumonialike organisms in 75 percent of females with various inflammatory diseases of the genito-urinary tract. Shepard[20] reports positive prostatic fluid cultures in 56 percent of 215 apparently normal males. Many other reports show remarkably variable percentages for the incidence of these organisms—all lower than the ones cited above. This seeming lack of accord may at least in part be accounted for by the difficulties encountered in isolation of the fastidious organisms. Harkness, et. al.[21] and Beveridge[22] considered the organisms directly related to many types of abacterial or nonspecific urethritis in the male. Gynecologic conditions have also been attributed to the pleuropneumonialike organisms.[23]

Pleuropneumonialike organisms and the "L"-phase organisms have been implicated in human disease on many occasions since 1937. Dienes and Smith in 1942[24] linked the pleuropneumonialike organisms to Reiter's syndrome which consists primarily of arthritis, conjunctivitis, and urethritis.

Numerous attempts since then have been made to establish incontrovertible evidence of the pleuropneumonialike organism etiology in nonspecific arthritis such as that of Reiter's syndrome and in rheumatoid arthritis. An interesting approach to this problem has been made by Brown, et al.[25] who treated over 150 patients having various rheumatic and collagen vascular diseases with aureomycin (chlortetracycline), terramycin (oxytetracycline), and chloramphenicol.

Since this group of diseases has been shown to be due to a type of hypersensitivity which in turn is influenced by cortisone, hydrocortisone, and ACTH, an antigenic material being released into the patient's body is suspected. This antigen in acute rheumatic fever only has been shown to be from beta-hemolytic streptococci but in certain other collagen diseases it could be from pleuropneumonialike organisms which are of low pathogenicity living in relative symbiosis with the patient and which were cultured from many of their patients.

On this assumption the antibiotics mentioned were given these patients and two different responses were obtained. One group tolerated the drug well and the majority showed definite clinical improvement, though prone to show relapse in four to 12 weeks; whereas, a second group developed under therapy exacerbations of joint involvement related to the type and amount of antibiotic given. Terramycin whose in vitro potency was greatest against the pleuropneumonialike organisms (25 times that of aureomycin) gave such adverse reactions in the latter group even in dosage as low as 10 mg. every three days orally. This dose was found to be the minimal amount of the drug

required to eliminate the pleuropneumonialike organisms from prostatic secretion. Abnormal serum proteins seemed to predispose to the undesirable type of reaction.

Antibiotic sensitivity

Susceptibility of the pleuropneumonialike organisms to the various antibiotics, excluding tetracycline, has been reported by several investigators.[25-27] Most of them agree that the in vitro as well as in vivo susceptibility of the organisms to the commonly used antibiotics which can be used to give safe, effective blood levels are as follows in descending order: Oxytetracycline, chlortetracycline, chloramphenicol, and streptomycin. It is of interest that the same order of hierarchy also reigns in clinical response of patients with nongonococcal urethritis. In a series of 736 such patients Harkness[21] reports cure rates as follows: Terramycin 86.5 percent, aureomycin 63 percent, streptomycin 39 percent, and chloramphenicol 36 percent.

Materials and methods

Specimens of prostatic secretions obtained by massage and vaginal secretions by aspiration were sent to the laboratory for smear and culture to detect the usual pathogens in addition to culture for pleuropneumonialike organisms. The smears were strained by Hucker's modification of Gram's method and examined microscopically under oil immersion. Blood agar (B.B.L. trypticase soy-agar with five-percent old blood-bank blood added) and Levine E.M.B. agar (Difco) plates and tubed Brewer thioglycolate medium (Difco) were the culture media used to detect the usual pathogens. The specimens for pleuropneumonialike organism cultures were collected in dry, sterile test tubes and inoculated on PPLO (pleuropneumonialike) agar (Difco) which contained one-percent PPLO serum fraction (Difco) and into PPLO broth (Difco) containing 25-percent ascitic fluid as well as the bacterial inhibitors potassium tellurite (Difco's Chapman tellurite solution) and crystal violet.[28] This broth was subcultured on PPLO agar plates after two days and after seven days' incubation at 37°C. All cultures were not reported negative until at least seven days' incubation had elapsed. Usually if growth of the pleuropneumonialike organisms was to occur it did so in 48 hours and was found on the initial agar plates. Identification was made by finding the typical colonies on the agar plates with the aid of the low-power lens of a microscope. The identical procedure was carried out on the control group.

In only a few cultures in each group was the initial agar culture negative while broth subcultures to agar were positive. Because of the incompleteness of the study of the effect of tellurite and crystal violet inhibitors on certain bacteria, namely production of the "L" phase, patients whose pleuropneumonialike organisms were isolated by broth subcultures only were excluded from this series.

Present study

In the course of a focus of infection survey on a patient admitted with a diagnosis of recurrent nongranulomatous iritis, chronic prostatitis was found and culture of his prostatic secretions revealed the presence of pleuropneumonialike organisms. Subsequently, consecutive patients admitted with a diagnosis of uveitis were studied from this standpoint. In addition to the usual topical therapy for the basic eye disease, these patients received either oxytetracycline or tetracycline 250 mg. four times daily for one week whenever pleuropneumonialike organisms were isolated from the prostatic or vaginal secretions. Repeat cultures were obtained following one week of chemotherapy with the antibiotic. Routine bacteriologic cultures for the usual pathogens were carried out on the same initial prostatic specimen and in all cases failed to reveal significant growth.

Thirteen patients with iritis or iridocyclitis and one with chorioretinitis juxtapapillaris were examined and seven of these

TABLE 1

RELATION OF PLEUROPNEUMONIALIKE ORGANISMS TO UVEITIS

Case No.	Age	Sex	Type of Uveitis	Previous Uveitis	Past History Arthritis	Prostate	Other Associated Conditions	Prostatic Culture Pleuropneumonialike Organisms
1	37	M	Nongran.	Iritis, 1954, O.U.	Recurrent Arthralgia	Chronic Prostatitis	None	Pos.
2	48	M	Nongran.	Iritis, 5 X Since 1941, O.U.	Rheumatic Fever 1951	Large and Boggy	None	Pos.
3	39	M	Gran.	Iritis 1955, O.U.	Arthralgia 1953	Normal	Multiple Sclerosis?	Pos.
4	58	M	Chorio-retinitis (Jensens)	None	None	Normal	Obesity	Neg.
5	30	M	Gran.	Iridocyclitis 3 X since 1950, O.U.	None	Normal	Syphilis 1949 Treated	Pos.
6	50	F	Nongran.	None	None	—	Perineal Abscess 1952 Cystitis and Pyelo-nephritis, 1954	Pos.
7	55	M	Nongran. (Traumatic)	None	None	Normal	None	Neg.
8	26	M	Nongran. (Traumatic)	None	None	Normal	None	Neg.
9	56	M	Nongran.	Iritis, 1951, O.D.	Acute Poly-arthritis 1941	Normal	Active Pulmonary Tuberculosis	Neg.
10	48	M	Nongran.	Uveitis, 1954, O.S.	Rheumatic Fever 1930	Boggy	None	Pos.
11	52	M	Nongran.	Keratitis Irido-cyclitis 1951, 1952, O.S.	None	Normal	Disciform Keratitis	Pos.
12	64	M	Nongran.	None	None	Boggy	Furunculosis of Arm	Neg.
13	64	M	Nongran. (Traumatic)	None	Osteoarthritis of Knees 3 yrs.	Enlarged and Boggy	None	Neg.
14	53	M	Nongran.	Iritis, 1936, 1944, 1955, O.U.	1936 Acute Migratory	Normal	Prostatitis 1936 TUR 1955	Neg.

had positive pleuropneumonialike organism cultures. Three of the negatives were in patients with iritis developing after direct eye trauma and one was in a patient with iritis associated with recurrent furunculosis of the arm from which Micrococcus aureus was isolated. A patient with active pulmonary tuberculosis who developed bilateral nongranulomatous iritis while under treatment with streptomycin (a known antipleuropneumonialike organism drug), proved to have negative culture, as did the sixth patient who had chorioretinitis.

In all the seven patients receiving the oxytetracycline, cultures of prostatic secretions became negative for the pleuropneumonialike organisms, in most instances simultaneous with the clearing of the iritis or iridocyclitis. One patient (5) with granulomatous iritis of long standing of presumptive tuberculous etiology remained unchanged even though the prostatic culture became negative. The second case (3) classified as granulomatous was less definitely so, the diagnosis being made largely on the type of keratic precipitates. This iritis which was of recent, precipitous onset, cleared promptly after treatment and was not accompanied by any Koeppe or Busacca nodules or permanent synechias. Vision returned to 20/20 each eye. Both these cases had pleuropneumonialike organisms cultured from their prostates before the antibiotic.

One of the patients (11) with positive prostatic fluid culture for the pleuropneumonialike organisms had iridocyclitis and disciform keratitis of unknown etiology. Prior to his most recent of three spontaneous

flareups of obstinate iridocyclitis and keratitis the eye had been quiet for three years. Marked but transient improvement was induced with typhoid vaccine fever therapy. Even after a course of tetracycline his culture remained positive though the organisms were reduced in numbers. Coincident with the administration of this antibiotic his corneal epithelial erosion in the disciform area began to grow and larger areas stained with fluorescein. Increase in anterior segment reaction was also noted. His serum proteins were normal. Consequently, this patient was treated with conjunctival flap, ACTH, and oxytetracycline simultaneously with good clinical result and eradication of the pleuropneumonialike organisms from the prostatic fluid. Since herpetic etiology could not be ruled out, steroid therapy was avoided until the conjunctival flap was placed.

Patient 14 was of particular interest in respect to his oculoprostatic relationship. His initial episode of nongranulomatous iritis in 1936 was related to prostatic massage for an obscure type of genito-urinary tract inflammation. In 1944 the recurrence of iritis did not appear to be related to the prostate; however, four days following a transurethral prostatectomy in 1955 he developed a severe bilateral iritis, again of nongranulomatous type. Pleuropneumonialike organisms could not be isolated from his prostatic secretion at his most recent attack which was of spontaneous onset without antecedent prostatic manipulation or recent sexual contact. The phenomenon of Shwartzman may be applicable to this situation where local ocular tissue hypersensitivity had been previously established from prostatic organism dissemination (? pleuropneumonialike organisms) and subsequently the same or related antigen from perhaps another source introduced intravenously incited the active inflammatory response of iritis.

Excepting the two granulomatous iritis cases the remaining were of nongranulomatous type, including five of those yielding pleuropneumonialike organisms on culture and having no other apparent etiology for their ocular disease. Only one of these five had clinical prostatitis but two had boggy, enlarged prostates. None had nonspecific urethritis clinically although urethroscopy was not done. Three had a history of arthritis in the past without association to present or previous uveitis. Four of the five had had previous episodes of iritis or iridocyclitis. Only the one female in this group had never had prior ocular inflammation.

Two of the patients with nongranulomatous disease received oxytetracycline initially, whereas three received tetracycline. In two of the latter group the organisms could not be cultured immediately after therapy but were present two to three months later even in the absence of iritis. These patients were then given prophylactic courses of oxytetracycline. At least in one of these patients venereal reinfection was probable. The other patient receiving tetracycline has been discussed. These findings suggest that oxytetracycline is superior to tetracycline in eliminating the pleuropneumonialike organisms from the prostatic secretions.

There definitely seemed to be a more rapid clinical improvement of the eye disease in most patients after beginning chemotherapy. Inadequate time has elapsed since therapy in this series to determine whether the recurrence rate of the iritis will be altered. One patient (6) had a mild recurrence three months after her initial episode which was treated with oxytetracycline. No pleuropneumonialike organisms could be cultured from vaginal secretions on this second occasion which suggests a similar mechanism as mentioned in regard to patient 14.

The control group consisted of 32 male patients without a history of uveitis and no clinical prostatitis or urethritis at the time of examination. Many of these patients, however, did have boggy, somewhat enlarged, but nontender prostates. Twenty-three of this group, or 72 percent, were

found to have the pleuropneumonialike organisms in their prostatic fluid obtained by massage and cultured similar to the other specimens.

Comment

The reports submitted are only suggestive of the role played by the pleuropneumonialike group of organisms in uveitis. It is possible that this relationship may be a direct one as in granulomatous uveitis but more probably it is indirect through the mechanism of hypersensitivity, as in the nongranulomatous type.[29]

Survey for existent foci of infection has become an established procedure in the diagnostic evaluation of a patient with uveitis although some skepticism has been voiced. It has long been recognized that arthritis and prostatitis which may frequently be abacterial by the usual culture methods may be associated with uveitis, especially iritis.

Favor,[30] in evaluating 36 cases of various eye diseases, including 21 with iritis, in regard to focus of infection, found four with clinical prostatitis. Nine (43 percent) of these patients with iritis and 30 percent of those with uveitis had or had had arthritis of some degree but this was not related directly to the clinical eye disease. Of the 33 patients on whom full data were recorded, 10 (30 percent) had a history of nonspecific urethritis, two had rheumatoid arthritis, and one, acute rheumatic fever. Cultures for pleuropneumonialike organisms were not done in his group. Other investigators have found a relationship between arthritis and iridocylitis not only in adults but also in children.[31, 32]

In Reiter's syndrome where pleuropneumonialike organism etiology is strongly suspected there have been a number of reports of iritis or iridocyclitis being present. In fact, in Reiter's original case report[33] his patient developed iridocyclitis, macular keratitis, and episcleritis two months after the initial symptom complex which included conjunctivitis. Dienes, et al.[3] report three cases of recurring iritis and one of keratitis in nine patients with Reiter's syndrome. Hollander, et al.[34] found two patients with superficial keratitis and one with moderately severe iritis in 11 patients with this syndrome. In a later series by Hollander[35] one of five cases had iritis which began as it did in Reiter's case about two months after initial conjunctivitis.

Others have reported a similar relatively high incidence of iritis in this syndrome. Weinberger and Bauer[36] note that ". . . Iritis in some patients has indicated probable recurrent activity in the absence of other manifestations. . . ." In perhaps the largest series of patients in one report (344 cases) Paronen[37] found 89 percent to have conjunctivitis, 6.4 percent iritis, and 7.8 percent keratitis. The iritis was of a fairly mild nongranulomatous type lasting three weeks to five months and was a rare initial finding. Usually, intraocular findings developed 10 days to 17 months after the initial conjunctivitis. This latent period is compatible with the time required to develop a hypersensitive state.

In view of the fact that most patients with this syndrome are under the exclusive care of urologists, the gross diagnosis of "episcleritis" so commonly reported in association with the conjunctivitis may in reality represent the ciliary vessel congestion of a mild self-limiting intraocular inflammation which could be ascertained only by use of the biomicroscope.

Morton, et al.[26] in 85 consecutive urology patients found 12 percent to have or to have had iritis but only one of these showed pleuropneumonialike organism growth from prostatic fluid.

Thus far, isolation of the pleuropneumonialike organism from the human eye has not been reported[3, 38] although they have been cultured from some animal conjunctivas as stated previously. Recently, in a patient with incomplete Reiter's syndrome, we

have grown the organisms from the conjunctival sac as well as from the prostatic fluid.

In this small series little can be inferred except that the pleuropneumonialike organisms are a possible cause of uveal disease through induced hypersensitivity. There is no satisfactory, practical way as yet whereby the presence and degree of hypersensitivity can be measured in regard to these organisms. No skin test has been reported using pleuropneumonialike organisms or an extract thereof. Serologic tests have been sporadically reported but thus far materials are not available for clinical use. Complement fixation in certain diseases due to pleuropneumonialike organisms shows a high initial titer which becomes insignificant in two to three months.[18]

The fact that such a large percentage of so-called normal men harbor pleuropneumonialike organisms in their genital tract does not necessarily militate against the etiologic role which pleuropneumonialike organisms may play under certain conditions. Many pathogenic organisms are known to be carried on the mucous membrane surfaces living in apparent symbiosis with the host but under favorable conditions these may cause disease either locally or in remote areas. We believe the pleuropneumonialike organisms to have such capabilities.

Now as in 1941 Guyton and Woods'[20] comment as to the etiology of nongranulomatous uveitis seems apropos: ". . . In most cases nongranulomatous uveitis can be explained on the basis of a local ocular sensitivity developing from a transient bacteremia. Such a transient bacteremia may arise from a clinically noninfected mucous surface as well as from a clinically infected surface. . . ."

Summary and Conclusions

1. The pathogenic potential of pleuropneumonialike organisms is reviewed, especially in regard to anterior uveitis.

2. Five cases of nongranulomatous uveitis with positive pleuropneumonialike organism cultures from the genital tract are reported. No other etiology for the iritis or iridocyclitis was found. These were treated with oral oxytetracycline (one gm. daily in divided dosage) in addition to the usual topical therapy and in all patients, the pleuropneumonialike organisms were eradicated coincident with clinical improvement of the ocular disease.

3. The recognized mechanism of hypersensitivity in nongranulomatous uveitis may be triggered by the release of antigens from the pleuropneumonialike organisms harbored asymptomatically in the genito-urinary tract. Only one patient in this series had symptomatic disease of the prostate. In another patient with negative pleuropneumonialike organism cultures, episodes of iritis were directly related to prostatic manipulation on two occasions.

4. Culture of prostatic fluid or vaginal secretion for pleuropneumonialike organisms seems advisable in focus of "infection" surveys. Oxytetracycline appears to be the most effective drug known against pleuropneumonialike organisms.

5. A practical, satisfactory method for evaluating the hypersensitivity status of patients to the antigens of pleuropneumonialike organisms is needed.

Box 3145 (14).

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EFFECT OF TOPICAL ANESTHETICS*

On regeneration of corneal epithelium

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The purpose of this investigation was to determine the effect of some of the more commonly employed topical anesthetics on the regeneration of the corneal epithelium of rat eyes.

It has been generally accepted that local anesthetics inhibit the healing process of corneal epithelium. In this study we attempted to determine whether some anesthetics had more delaying effect than others. If two anesthetics were equal in other properties, such as potency, rapidity of action, stability, and freedom from irritation and allergic reactions, it would be preferable to employ the drug having the least detrimental effect upon the regeneration of the corneal epithelium.

Gundersen and Liebman[1] determined experimentally the effect of various local anesthetics on the regeneration of corneal epithelium in guinea pigs. Identical abrasions were made in each eye of the animal and the right eye was treated with the anesthetic hourly while the untreated left eye served as a control.

The drugs employed in their experiments were fresh preparations similar to those in daily clinical use. The anesthetics which they studied were four-percent cocaine hydrochloride, 10-percent cocaine hydrochloride, one-percent butacaine sulfate, four-percent larocaine hydrocloride, one-percent phenacaine hydrochloride, and 0.5-percent tetracaine hydrochloride all containing 0.5-percent chlorobutanol.

One-percent phenacaine hydrochloride and 0.5-percent tetracaine hydrochloride were thought to be the least toxic to the regenerating epithelium. One-percent butacaine sulfate, four-percent larocaine hydrochloride, four-percent cocaine hydrochloride, and 10-percent cocaine hydrochloride seemed to show an increasingly inhibitory effect, in the order named.

Gundersen and Liebman also investigated the effect of pH on the regeneration of corneal epithelium. The influence of pH alone was studied by the use of a buffer without an anesthetic, and it was found that a buffer solution at pH 2.82 exhibited a definite inhibitory effect on the regeneration of the corneal epithelium, whereas, buffer solutions with a pH of 4.12 or 6.28 had no effect.

In one of our previous publications,[2] butyn and pontocaine, as well as several antibiotics, were studied, using a different technique from the one employed in the study reported here. In the earlier work rats were anesthetized with ether and 30 small circular epithelial injuries were produced in each cornea with a fine-pointed needle. The eyes were

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then enucleated and placed in the various solutions to be tested. The solutions were kept at a constant temperature of 38°C. and continuously aerated for three hours by bubbling air through the solutions. The pH was maintained at 7.2 by using one of Sörensen's phosphate buffer mixtures as the solvent.

The epithelial defects healed completely after three hours in the buffer solution but no healing occurred in the eyes which were immersed for three hours in the buffer solution containing two-percent butyn or 0.5-percent pontocaine.

This paper presents the effect of several topical anesthetics on the repair of small epithelial defects in the rat's cornea, using a technique devised by Friedenwald and Buschke.[3]

Procedure

Young, adult, white rats were used in all experiments. The anesthetic solution was placed in the right eye, while the left eye, which served as the control, received either distilled water or physiologic saline. The anesthetic compounds were dissolved in either distilled water or physiologic saline. Whichever solvent was used served as the control.

One drop of the anesthetic solution was placed in the right eye of an unanesthetized rat at 10-minute intervals for 30 minutes (three administrations). A similar amount of the control solution was placed in the left eye at the same time intervals. The rat was anesthetized with ether. With a fine-pointed needle 30 small circular epithelial injuries were produced in each cornea. One drop of the test solution was then placed in the right eye every 15 minutes for three hours (11 administrations). The control solution was placed in the left eye at the same intervals. At the conclusion of the treatment the rat was again anesthetized, killed, and the eyes enucleated. Three or more rats were treated with each anesthetic solution.

The enucleated eyes were placed in a mixture of formalin and alcohol for fixation. The cornea was removed from the eye and cut into three parts. The three portions of cornea were stained with Harris' hematoxylin, cleared, and mounted on a slide in Canada balsam with the epithelial side uppermost.

The stage of healing of the epithelial defects was observed with the high dry power of the microscope (×550). An unhealed puncture showed an uncovered defect in the epithelium surrounded by cells whose nuclei do not show an increased staining reaction and the cells are arranged in a tangential pattern rather than a radial fashion to the lesion (fig. 1).

In punctures which showed the first stage of healing some cells were found in the basal layer in a radial pattern covering part of the floor of the lesion (fig. 2). In defects which showed the second stage of healing the floor of the lesion was completely covered by epithelium and the nuclei of cells in the superficial layer were arranged in a radial manner (fig. 3). A healed lesion was characterized by the presence of epithelial cells

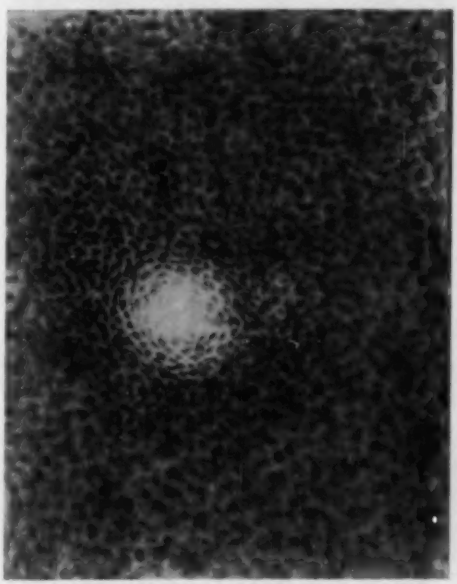

Fig. 1 (Marr, et al.). An unhealed puncture.

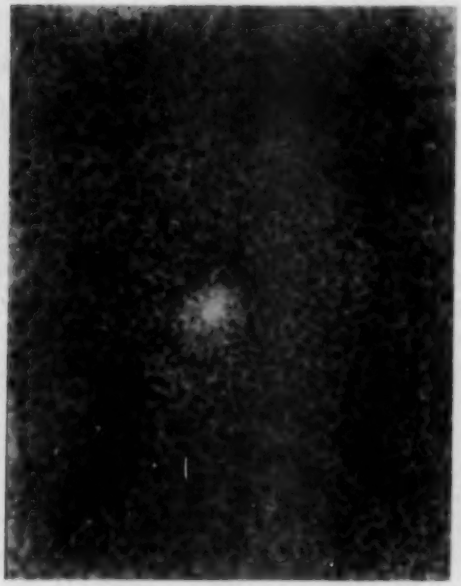

Fig. 2 (Marr, et al.). Puncture showing first stage of healing.

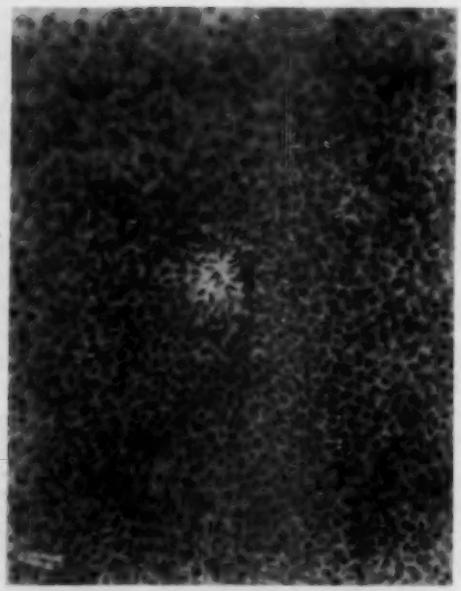

Fig. 3 (Marr, et al.). Defect showing second stage of healing.

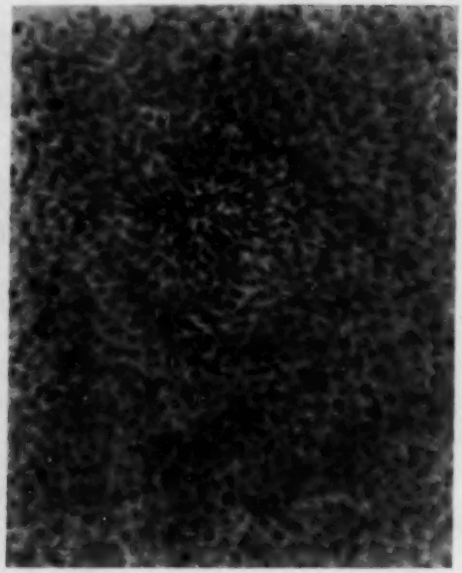

Fig. 4 (Marr, et al.). A healed lesion.

in both the basal and superficial layers and by an increase in the staining of the nuclei of the cells (fig. 4).

The number of lesions in each stage of healing was recorded for the treated eyes and for the control eyes. The control eyes all showed the majority of lesions to be in the second stage of healing with the remainder healed. The healing was not quite as advanced in the eyes receiving distilled water as in those receiving physiologic saline, presumably due to the hypotonicity of the distilled water.

Anesthetics were classified according to the stages of healing they permitted as described above. Anesthetics which permitted the same degree of healing as the controls were classified as permitting normal healing. Anesthetics which delayed but did not completely inhibit healing were classified according to the stage of healing shown by the majority of the lesions.

The pH was determined on all the anesthetic solutions studied. These varied from pH 4.3 to 6.8. Hydrogen-ion concentration in this range does not have an inhibitory effect

on the regeneration of corneal epithelium according to the work of Gundersen and Liebman[1] and some of our previous work.[4]

Amylsine* (naepaine) is a derivative of para-aminobenzoic acid and was supplied as the hydrochloride in crystalline form. The crystals were dissolved in physiologic saline to make a two-percent solution. The pH was 5.3.

Butyn (butacaine sulfate) is the dibutylaminopropyl ester of para-aminobenzoic acid and was supplied as the sulfate in tablet form. The tablets must be dissolved in distilled water as saline solution will cause precipitation. A two-percent solution was used and the pH was 5.5.

Cocaine is a naturally occurring ester of benzoic acid and was used as the hydrochloride dissolved in distilled water to make a four-percent solution. The pH was 4.3.

Dorsacaine (benoxinate hydrochloride) is one of the newer topical anesthetics. The compound was developed in Switzerland, where the hydrochloride salt is known as Novesine. Dorsacaine is a benzoic acid ester supplied as a white powder which is readily soluble in water to form a clear, stable solution. A 0.4-percent solution is recommended for routine office use and is the concentration which we studied. The pH was 5.6.

Holocaine (phenacaine) was supplied in powder form as the hydrochloride. It differs greatly in chemical structure from the majority of local anesthetics and is a derivative of phenetidin. Holocaine was used as a one-percent solution in water and the pH was 5.9.

Metycaine (piperocaine) was received in powder form as the hydrochloride. Metycaine is an ester of benzoic acid and a base containing nitrogen in the form of a methylpiperidine ring. Saline was used to make a two-percent solution and the pH was 4.6.

Nupercaine (dibucaine) is a complex amine derivative of quinoline and was dissolved in water to make a 0.1-percent solution. The pH was 5.5.

Ophthaine also belongs to the group of the newer topical anesthetics. It too is a benzoic acid ester and is freely soluble in water. The commercial preparation is 0.5 percent and we prepared the same concentration by dissolving the powder in water. The pH was 5.9.

Pontocaine (tetracaine) is another derivative of para-aminobenzoic acid. It is one of the more widely used topical anesthetics, and the commercial preparation is 0.5-percent in saline solution. We used the same concentration in normal saline and the pH was 5.6.

Xylocaine (lidocaine), synthesized by Lofgren in 1943, is one of the more recent of the local anesthetics. It is unique among local anesthetic agents in that chemically it is an aminoacylamide. Russell and Guyton[5] reported on the use of Xylocaine in ophthalmic surgery in 1954. In our work a two-percent aqueous solution of xylocaine hydrochloride was studied and the pH was 6.8.

Results

As is shown in Table 1 no healing occurred with Amylsine. When butyn was used no regeneration of the epithelium occurred and the epithelial layer appeared to be loosened from the underlying membrane. Cocaine prevented healing of the epithelial defects and there was some drying of the epithelium. No healing occurred in the eyes treated with Dorsacaine and there was some drying of the epithelium. No healing occurred with Holocaine. The eyes treated with Metycaine showed normal healing. No healing occurred with Nupercaine. Ophthaine prevented any regeneration of the corneal epithelium. The eyes treated with Pontocaine showed healing predominantly in the second stage and the remaining lesions were in the first stage of healing. Normal healing

* We wish to thank the following companies for generously supplying the indicated material: Novocol Chemical Company, Amylsine; Abbott Laboratories, Butyn and Holocaine; Smith-Dorsey, Dorsacaine; Eli Lilly & Company, Metycaine; Ciba, Nupercaine; Squibb, Ophthaine; Winthrop-Stearns, Pontocaine; Astra, Xylocaine.

TABLE 1

RESULTS OBTAINED WITH VARIOUS ANESTHETICS

Anesthetic	%	No Healing	1st Stage Healing	2nd Stage Healing	Normal Healing
Amylsine	2	+			
Butyn	2	+			
Cocaine	4	+			
Dorsacaine	.4	+			
Holocaine	1	+			
Metycaine	2				+
Nupercaine	.1	+			
Ophthaine	.5	+			
Pontocaine	.5			+	
Xylocaine	2				+

of the epithelial defects occurred in the eyes treated with Xylocaine.

SUMMARY

Using a technique devised by Friedenwald and Buschke, the effect of various topical anesthetics on the healing of epithelial defects in the rat's cornea was studied. Amylsine, butyn, cocaine, Dorsacaine, Holocaine, Nupercaine, and Ophthaine in the concentrations described prevented healing of the epithelial lesions. Pontocaine delayed healing slightly and normal regeneration of the epithelium occurred with Metycaine and Xylocaine.

The Johns Hopkins Hospital (5).

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OPHTHALMIC MINIATURE

My business was to meet Mr. Boyle, which I did, and discovered about my eyes; and he did give me the best advice he could, but refers me to one Turberville (Daubigny, 1611-1696) of Salsbury, lately come to town, which I will go to.

Pepys' Diary, June 22, 1668.

THE EFFECTS OF NONABSORBABLE INTRASCLERAL SUTURES*

ON THE GROWING ALBINO RABBIT EYE

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This investigation is an analysis of the effects, on a growing eye, of nonabsorbable sutures placed intrasclerally.

The rabbit was selected for this study because of the following factors:

1. The rabbit eye and orbit permit extensive intrascleral suturing when the animal is but a few weeks old.

2. The scleral vasculature is discrete so that the sclera may be manipulated with minimal bleeding.

3. The globe increases markedly in diameter during the first few months of life.

To obtain a homogeneous group of animals, only albino rabbits obtained from the same dealer were used.

DIAMETERS OF EYE IN ALBINO RABBITS

The anterior-posterior and medial-lateral diameters of freshly enucleated eyes from living rabbits were measured. Live animals, rather than dead animals, were used to minimize softening of the globe prior to study.

The relation of animal age and weight to diameters of the globe is shown in Table 1.

Repeated measurements of the same diameter with a caliper by the same and different observers yielded consistent readings plus or minus 0.3 mm.

The medial-lateral diameter is consistently greater than the anterior-posterior diameter. The eye of the albino rabbit is thus flattened in the anterior-posterior dimension. The largest eye enucleated measured 20 mm. by 18 mm. It was obtained from a 28-week-old, 3,750-gm. animal (table 1). The smallest eye enucleated measured 11 mm. by 10 mm. It was obtained from a 10-day-old, 155-gm. animal (table 2).

INCREASE IN EYE SIZE IN LITTER MATES

Litter mates were killed at short intervals following birth. The rapid growth of the albino rabbit eye in the early developmental period is shown in Table 2.

Growth of the albino rabbit eye is virtually complete by the 23rd week. The average weight of the albino rabbit at this age is 3,000 gm. The diameters of the eyes in animals aged 23 weeks to 125 weeks varied between 18 and 20 mm. in the medial-lateral direction and between 16.25 and 18. mm. in the anterior-posterior direction.

EXPERIMENTAL PROCEDURE

Fifteen albino rabbits, aged five to seven weeks, weighing from 900 to 1,200 gm., were used to determine the effects of nonabsorbable intrascleral sutures. Their eyes were enucleated when 25 weeks old.

Anesthesia was obtained by intravenous veterinary sodium pentobarbital (Nembutal) and topical tetracaine hydrochloride (Pontocaine).

An external canthotomy was done. Intrascleral catgut sutures were inserted at the limbus in the 3-, 9-, and 12-o'clock positions to stabilize the globe. The conjunctiva was dissected at the limbus from the superior portion of the sclera. The superior rectus and superior oblique muscles were detached at their insertions and allowed to retract into the orbit. They were not reattached subsequently.

Intrascleral sutures of either plain catgut or black silk were placed in the sclera as shown in Figure 1. Each silk or gut intrascleral suture was re-enforced at each angle with a black silk suture. Eight silk sutures for subsequent measurements were then inserted into the sclera. They are labelled "silk markers" in Figure 1.

The operative procedure was identical in

* From the Section of Ophthalmology of the University of Chicago. I am grateful to Dr. Frank W. Newell for his suggestions.

TABLE 1

RELATION OF ANIMAL AGE AND WEIGHT TO DIAMETERS OF GLOBE

	Age (wk.)	Weight (gm.)	Right Eye		Left Eye	
			Medial-Lateral Diameter (mm.)	Anterior-Posterior Diameter (mm.)	Medial-Lateral Diameter (mm.)	Anterior-Posterior Diameter (mm.)
1.	6.0	1,100	15.00	14.00	15.00	14.25
2.	8.0	1,423	15.25	14.50	15.50	14.50
3.	22.5	2,775	18.25	17.50	18.75	17.25
4.	23.5	3,100	18.00	17.50	18.00	17.25
5.	24.5	3,030	18.50	17.00	18.50	17.00
6.	25.5	2,985	18.00	16.25	18.25	16.75
7.	26.5	3,165	18.25	16.25	18.50	16.75
8.	26.5	3,255	18.25	16.50	18.25	16.50
†9.	23.0	2,800	18.50	17.50	19.00	17.50
*10.	5.0	825	14.50	13.50	14.50	13.50
*11.	7.0	1,350	15.50	14.50	15.50	14.25
12.	24.0	2,880	18.00	16.50	17.75	16.50
13.	28.0	3,075	18.25	16.50	18.25	16.75
*14.	20.5	2,920	18.00	16.50	18.00	16.50
*15.	22.5	3,065	19.00	17.00	19.00	17.00
16.	28.0	3,750	19.50	18.00	20.00	18.00
17.	9	1,510	15.75	14.00	15.50	14.50
18.	26	3,200	18.50	18.00	18.50	17.50
19.	125	5,465	19.00	18.00	19.00	18.00

* Litter mates.
† Mother of litter (1-8).

all eyes except for the use of catgut in the control eye and black silk in the opposite eye.

A No. 85, five-mm. Grieshaber needle was used for all intrascleral suturing. Ethicon black braided silk, size 6-0, was used for the continuous intrascleral sutures in the experimental eye and for the markers and re-enforcing knots in the experimental and control eyes. Ethicon surgical gut, plain, size 6-0, was used for the continuous intrascleral sutures in the control eyes.

The distance a,a′ was measured by placing a silk suture on the surface of the globe from point a to point a′ at a constant distance from the limbus. This suture was measured subsequently with a vernier caliper.

The conjunctiva was reattached at the

TABLE 2

GROWTH OF EYE OF ALBINO RABBIT

	Age of Litter Mate (days)	Weight (gm.)	Right Eye		Left Eye	
			Medial-Lateral Diameter (mm.)	Anterior-Posterior Diameter (mm.)	Medial-Lateral Diameter (mm.)	Anterior-Posterior Diameter (mm.)
1.	10	155	11.25	10.0	11.0	10.0
2.	17	297	13.0	11.5	12.8	11.2
3.	24	463	13.9	12.7	13.6	12.5
4.	30	680	13.5	12.9	13.8	12.9
5.	41	1100	15.5	14.2	15.3	13.7

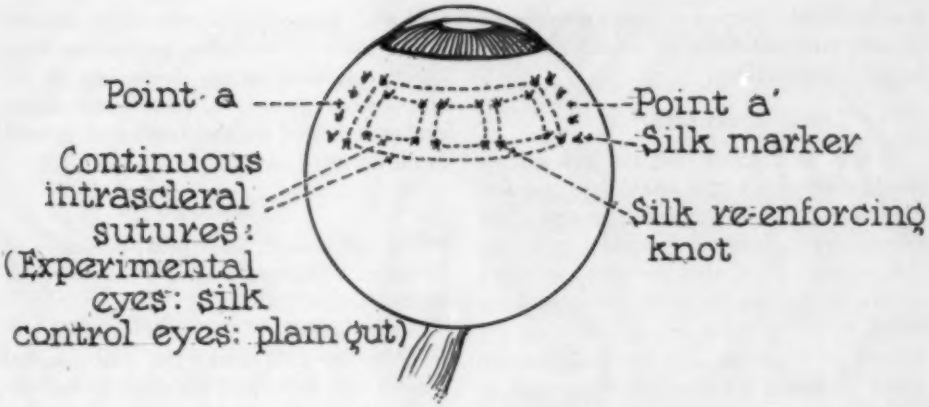

Fig. 1 (Land). Suturing technique.

limbus with the sutures which were used to stabilize the globe throughout the operative procedure. The canthotomy was then closed.

The canthus and conjunctiva were well healed within 10 days at which time the silk sutures could be seen distinctly through the conjunctiva. These sutures became increasingly indistinct during the subsequent two months and at the time of enucleation this material could not be seen beneath the conjunctiva in most of the animals.

Results

The eyes were enucleated from anesthetized animals when 25 weeks old.

The orbital contents were dissected close to the orbital bones and removed en bloc. The globe was freed cautiously from the surrounding structures.

There was no distortion of contour and no scleral wrinkling or buckling seen on gross inspection and with loupe magnification.

In no animal was the entire set of silk intrascleral sutures, re-enforcing knots, and markers seen grossly or with loupe magnification. In areas where silk sutures were known to have been placed intrasclerally, fine dark lines were seen frequently. Teasing of the sclera over these lines did not reveal any silk fibers. Only a few of the silk markers and re-enforcing knots were found in the control eyes.

Since many markers were not found, valid measurements between them were not possible.

Measurements of the diameters of these globes showed a range of 18 to 20 mm. in the medial-lateral direction and 16.25 to 18 mm. in the anterior-posterior direction. This is the same range of diameters as in nonoperated eyes (table 1).

Thirty eyes, 15 in which intrascleral catgut had been placed and 15 in which intrascleral black silk had been placed, were studied microscopically. The eyes were fixed in Zenker's solution. Anterior and posterior calottes were made so as not to disturb the operative area. Following celloidin embedding, sections 17 microns thick were made and stained with hematoxylin and eosin.

Microscopic examination of the control eyes revealed no remnants of gut suture material. The control procedure had no microscopically demonstrable effect on the albino rabbit sclera.

In eyes in which continuous intrascleral silk sutures had been inserted the suture material appeared in numerous sections. It was located within the sclera and none had penetrated to the deeper structures. The silk fibers were surrounded by aggregates of lymphocytes and there were occasional giant cells present.

No buckling or distortion of scleral fibers

was observed. There was no microscopically demonstrable alteration of the scleral fibers in any of the sections.

Discussion

It was anticipated that the gut sutures would disappear within a few days and that they would not affect ocular growth. Two effects were believed possible with the silk sutures. First, that the sclera enclosed within the boundaries of the intrascleral sutures would wrinkle or buckle with the growth of the globe. The practical impossibility of fixing a suture tightly enough to prevent slipping without causing necrosis made likely the second possibility, that the sclera enclosed within the silk sutures would grow unhindered and would not wrinkle or buckle.

It was impossible to measure the enclosed areas following maturation of the animals and it cannot be definitely asserted that there was no interference with growth in the operated area. However, the over-all dimensions of the operated eyes after enucleation were exactly the same as the dimensions of the nonoperated eyes. Additional microscopic studies indicated no abnormality of growth in the operated area.

Summary

The age, weight, and eyeball diameters of 19 animals indicate a close relationship of these variables (table 1).

Normal growth of the eye is virtually complete by the 23rd week. The medial-lateral diameter of the eye of the adult albino rabbit is 18 to 20 mm. The anterior-posterior diameter is 16.25 to 18 mm.

Silk sutures and catgut sutures were placed intrasclerally in five- to seven-week-old albino rabbits. The eyes were enucleated at the age of 25 weeks. No gross or microscopic effect on the development of the globe could be demonstrated.

Philadelphia General Hospital (4).

Ophthalmic Miniature

In seven cases of extraction of cataract I have employed fluorescein, at varying periods after operation, to see when the edges of the conjunctival flap (after cataract extraction) cease to stain. I found staining in one case completely absent on the sixth day; on the other hand I have found staining present as late as the eighteenth day. It is a method of investigation worthy of more extended and careful observation.

Treacher Collins, *Tr. Ophth. Soc. U. Kingdom*, **34**:20, 1914.

NOTES, CASES, INSTRUMENTS

OSTEOMA OF THE ORBIT

Report of a case

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Orbital osteomas are rare. There are some 400 cases recorded in the literature. Reese[1] studied 109 cases of tumors arising primarily in the orbit and found osteoma in only one case. Forrest[2] in a similar report of 184 cases found only five. Duke-Elder[3] states that no part of the skeleton is more prone to ossa hypergenesia than the orbit where so many bones are so intimately related and this is the most probable etiology; however some have postulated a periosteal origin.

The most frequent location of osteomas is the upper inner angle of the medial wall, as in the case reported. It is believed that they originate from the lining of the sinuses and invade through the wall of the orbit. Histologically they are of two types (1) hard or elevated and (2) soft or cancellous. Small new-growths of the orbit are of little clinical significance and are symptomless until they become of such size as to displace the globe and produce exophthalmos; therefore they are classified as benign. However, if they reach sufficient size, they may take on malignant clinical characteristics. Osteomas are often found accidentally during X-ray studies of the sinuses. They are thought to originate at an early age and remain unnoticed until 20 to 30 years of age and even then may produce few or no symptoms, as in the case reported.

Case report

History. A Negress, aged 48 years, was referred because of a firm growth located at the inner canthal area of the right eye. Her only complaint was an occasional pain in the region of the mass and infrequent lacrimation. For the past two years she had known the presence of the mass and felt that it had grown larger during the past year. There was no history of injury to the area. Her family and personal history were noncontributory.

Examination. The patient was a well-nourished woman who presented a hard palpable mass located at the inner canthal area of the right eye. The visual acuity was 20/20 in each eye. No intraocular disease was present and the fundus was normal in each eye. There was no exophthalmos since the new-growth was located more anteriorly. The extraocular muscular movements were normal. The large firm mass was palpable in the upper inner quadrant of the orbit and could be palpated along the entire medial rim and some 10 mm. along the margin of the floor of the orbit. It was not attached in any way to the globe. There was no palpable mass in the left orbit. The roentgenogram report (figs. 1 and 2) was:

Right orbit. Anteroposterior lateral

Fig. 1 (Hobbs). Anteroposterior X-ray film, showing the osteoma in the medial wall of the right orbit.

FIG. 2 (Hobbs). Lateral X-ray film, showing the osteoma.

Water's optic foramen view. Bony density somewhat lobulated located medially in the right orbit. Measures 2.7 by 1.4 cm. Projected 1.5 cm. anterior to optic foramen. Lateral to ethmoid air cell on anteroposterior view, minimal if any haze in ethmoid region. Projected superior and medial to maxillary sinus on Water's view. No X-ray proof of involvement of the sinus itself. Goalwin technique measurements of diameters of right optic foramen show no abnormality. No evidence of bony destruction in region of right optic foramen.

Left orbit. A five-mm. round density of similar quality is projected over the left frontal sinus region on these views.

Impression. (1) The radiographic appearance is that of an orbital osteoma or fibro-osteoma. (2) The density in left frontal sinus region has the appearance of small osteoma.

Hospitalization. Her general physical condition and laboratory studies were within normal limits. Under thiopental sodium (Pentothal®) anesthesia the lesion was removed.

Operative procedure. After preparation and drape of the right eye area a retrolinear incision two cm. in length was made in the nasal angle above the inner canthal ligament. The structure was easily exposed beneath the medial canthal ligament without severing it. It was ivorylike in appearance and markedly lobulated (fig. 3).

An Allis forceps was placed on the growth and with a gentle rocking back and forth the entire structure was broken off and removed. The surface of the new-growth was smooth except a small area at its attachment to the ethmoid bone. This area was smoothed with a periosteal elevator. Bleeding was controlled with bone wax. The skin incision was closed with interrupted sutures and a pressure dressing applied. The patient had no postoperative complications and was discharged after the third day of hospitalization.

Pathologic report. Gross: The specimen consists of an irregular portion of bone showing an area of detachment which measures 18 mm. in maximum length and 11 mm. in width. The bone per se is a bosselated nodular structure which measures 31 by 21 by 20 mm. Sectioning shows the surface to be dense, solid bone. Microscopic: Sections show dense cortical bone arranged in the pattern of an osteoma. There is no evidence of inflammation or degeneration.

Diagnosis. Osteoma.

Fig. 3 (Hobbs). Showing the osteoma at surgery.

Postoperative care. The skin sutures were removed on the sixth day. There was no undue reaction to the surgery and the recovery was uneventful.

Summary

A case of osteoma arising from the right ethmoidal region is reported. There was also a small similar lesion in the area of the left frontal bone not large enough to require removal. Adequate exposure was obtained by making the incision above the inner canthal ligament and the patient had an uneventful recovery following removal of the new-growth.

213-215 Martin Building.

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OPERATIVE CORRECTION OF SENILE ENTROPION

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The mechanism of the development of spastic entropion must be clearly understood, as it explains the etiology of the deformity of the eyelid and dictates the technique for the corrective operative procedure.

Senile atrophy will not only cause a backward displacement of the eye, but a slackening and elongation of the orbicularis muscle. These two factors will change the normal physiologic relationship between the eye and the eyelid. When the patient closes his eye tightly, the central portion of the orbicularis which is stronger will invert the eyelid, as shown in Figure 1. The frequently used thermocautery needling along the lower edge of the tarsal plate may improve entropion but not infrequently a surgical correction is necessary. Wheeler,[1] in 1938, described an operation for entropion with shortening of the orbicularis muscle along the lower edge of the tarsal plate.

The following modification of the operative procedure has been found to be very easy and successful.

Operative procedure

The skin incision is made along the upper edge of the eyelid, below the eyelash line. A sharp small pointed scissor is used to dissect the skin downward, and widely medially and laterally. The muscle is then freely separated from the tarsal plate. The orbicularis, which is now free, is cut in the middle obliquely from the upper edge to the level of the lower edge of the tarsal plate, as shown in Figure 2. The free ends of the divided muscle are adjusted with two pairs of tissue forceps in such a way that the eyelid is placed in a normal relationship to the eye. One fine catgut suture is used to secure the upper edge. The shortening along the upper portion may be approximately one or two mm. with an overlapping of the muscle.

Fig. 1 (Szlazak). Typical senile entropic eyelid.

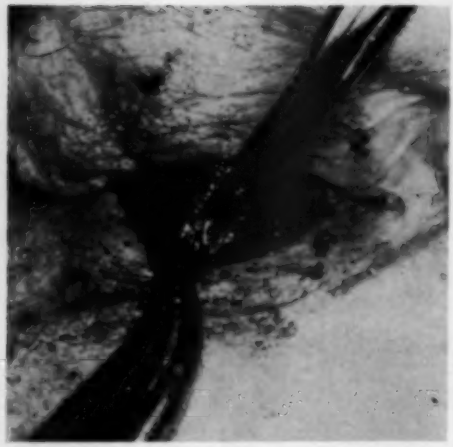

Fig. 2 (Szlazak). Illustrates the oblique division of the orbicularis muscle on the whole width, held by mosquito forceps.

Using tissue forceps again, the lower edges of the muscle are adjusted, so that they will have a normal pressure on the lower edge of the tarsal plate. Two sutures of fine catgut are then tied at this level, each one on the free end at the line of division, and corresponding with the overlapping portion of the muscle. In this way, the divided orbicularis is secured by three catgut sutures, one at the top and two at the bottom, and the overlapping portion of the muscle will nearly form a right angle. If the overlapping along the upper edge should require a slight shortening only, the lower portion of the muscle, which is thinner, will be shortened considerably.

Fig. 3 (Szlazak). After suturing of the skin intradermally.

Fig. 4 (Szlazak). Final result.

The skin is then sutured intradermally with 5-0 nylon with the free ends secured by a small adhesive tape to the cheek, as shown in Figure 3. The suture will be removed in four or five days (fig. 4).

Summary

The operative correction of senile entropion is presented with shortening of the orbicularis muscle in its whole width and thickness. The skin incision is made near the edge of the eyelid, so that when healed will result in an inconspicuous scar. The shortening of the orbicularis along the upper and lower edges will restore a normal physiologic relationship between the eye and the eyelid. The shortening along the upper edge is to a lesser degree than that at the lower edge, which presses on the tarsal plate. An oblique division of the muscles gives a better adjustment for a shortening, and the overlapping edges of the divided and sutured muscle will form a stronger support, without causing the eyelid to bulge.

2125 11th Avenue.

References

1. Wheeler, J. M.: The use of the orbicularis palpebrarum muscle in surgery of the eyelid. Am. J. Surg., **42**:7, 1938.

POOL GONIOSCOPY

OFFICE TECHNIQUE OF SIMPLIFIED ANTERIOR CHAMBER VISUALIZATION

JACK P. COWEN, M.D.
Chicago, Illinois

A simple study of the angles of the anterior chamber, particularly in all cases of glaucoma, can be accomplished by a lens-free method of flooding the inner angle of the eye with saline solution and of studying the submerged chamber angle with flashlight illumination and with simple five to 10-power loupe magnification. The detached head of the binocular slitlamp makes an excellent magnifying and viewing instrument, as would a Troncoso[1] monocular or binocular hand-grip magnifier.

This simplified method of viewing the filtration angle was suggested by the work of Mizuo,[2] who, in 1914, visualized the lower chamber angle by instilling water in the lower cul-de-sac. He based his method on the Czermak water-filled orthoscope, a primitive open contact glass through which Czermak viewed the fundus in 1851. Grönholm[3] in 1903 measured the anterior chamber depth by a similar eyebath arrangement.

The advantages of this simplified pool-gonioscopy method are as follows:

1. Extreme adaptability to all patients with a minimum of special and expensive equipment.

2. The lack of frightening instrumentation and introduction of lenses between the tense lids of an already apprehensive glaucoma patient.

3. The absence of problems of air bubbles and of refilling partially empty contact glasses with syringes which may produce conjunctival pain and subconjunctival hemorrhages by accidental lacrimal-needle manipulations.

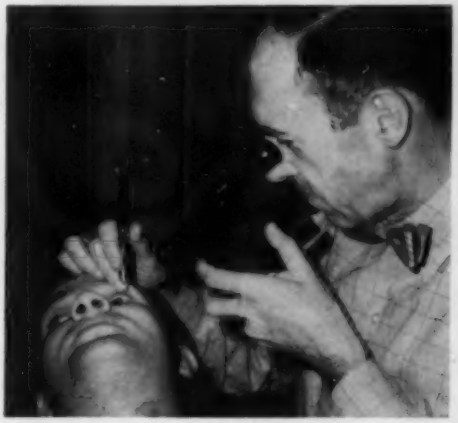

Fig. 1 (Cowen). Illustrating the technique.

The disadvantages of this method are obvious:

1. Limited visualization of the nasal half of the chamber angle only is permitted. Perhaps vertical angles can be seen by filling the fornices with saline solution and using Mizuo's technique for visualizing these areas.

2. Less magnification is obtainable than when a curved-surfaced Koeppe-type[4] modern contact glass and slitlamp[5] can be used.

3. Supine position with steady position of the head and extreme version of the eyes to submerge the angles below the fluid level are necessary.

4. Low-bridged nose individuals, like Negroes and Orientals, make the filling of the pool at the inner angle of the nose difficult.

111 North Wabash Avenue (2).

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1. Troncoso, M. U.: Gonioscopy and its clinical applications. Am. J. Ophth., **8**:433, 1925.
2. Mizuo: Ein Verfahren zur Besichtigung der Kammerbuct. Klin. Monatsbl. f. Augenh., **25**:561, 1914.
3. Grönholm: Eine einfache Methods der vorderen Augenkanmer zu messen. Skand. Archiv. f. Physiolog., **14**:235, 1903.
4. Berliner, M.: Biomicroscopy of the Eye. (Gonioscopy by H. S. Sugar, M.D.) New York, Hoeber, 1943, v. 1, Chap. 17.
5. Sugar, H. S.: The Glaucomas. St. Louis, Mosby, 1951, Chap. 20.

SCREENING TEST FOR ANISEIKONIA

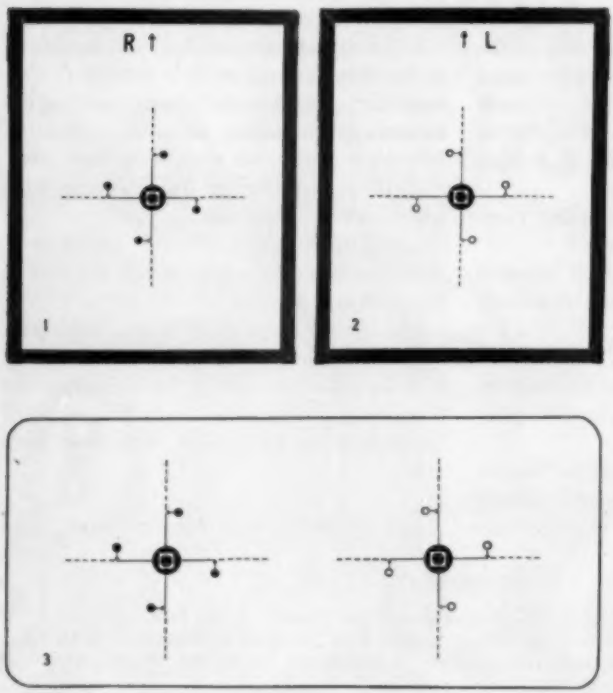
RONALD M. BURNSIDE, M.D., AND CHARLOTTE LANGLEY
Dallas, Texas

Patients with suspected aniseikonia may be screened on the major amblyoscope or stereoscope to determine if a more complete evaluation on the eikonometer is indicated.

The target for the amblyoscope is as shown in Figures 1, 2, and 3. The slide for the right eye consists of a horizontal and a vertical line drawn perpendicular to each other; at the intersection of the two lines there is a square with a large black circle; equidistant from this central fixation point there are four black dots with arrows. Two of the arrows are on the 90-degree meridian and two on the 180-degree meridian. The slide for the left eye is basically the same except that directly opposite, but in a corresponding position, there are four circles with arrows.

When the patient is looking through the amblyoscope, he will fuse the center square and circle and if there is no appreciable size difference, the arrows of the black and white dots will coincide. The dash or broken lines at the terminal ends of the lines may give an approximate percentage of size difference to be expected; each dash corresponds to one degree. If an amblyoscope is not available, the same target has been transferred on a card for use in the stereoscope. Slight errors in the reproduction of the targets or lens error in the instruments may be checked and noted by the examiner.

4105 Live Oak Street (25).



Figs. 1, 2, and 3 (Burnside and Langley). (Figs. 1 and 2) Slides for amblyoscope. (Fig. 3) Card for stereoscope.

SINGLE-DOSE STERILE UNIT FOR OFFICE USE

EUGENE ELKIN, M.S.
Riverside, California

Solutions of fluorescein sodium have been found to be fertile media for the growth of Pseudomonas aeruginosa.[1] This organism is capable of producing serious ocular infections.[2,3]

Considerable difficulty has been experienced in maintaining the sterility of these solutions in ordinary dropper bottles since bacteria from the air or a chance contact with the eyelashes can produce a serious contamination.

Filter paper impregnated with fluorescein which has been autoclaved is now widely used. However, on certain occasions more intense staining is desirable.

An answer to this problem would be to prepare the solutions in single-dose containers. Unfortunately, most single-dose containers are unsuitable for ophthalmic solutions.

I have improvised a very simple container (fig. 1) which can be made from material found in any pharmacy. It can be easily autoclaved and can be used repeatedly. This container consists of an ordinary straight medicine dropper and an extra rubber bulb. The dropper is filled with freshly prepared fluorescein solution, is inverted with the bulb side down and the second bulb is then slipped over the open end. The assembly is then autoclaved and can be kept in the office until needed.

It is advantageous to use bulbs of different colors in order to identify the bulb which is to be removed. Droppers with an untapered end are the most convenient since they can be inverted repeatedly and the solution will still flow back into the glass cylinder. With tapered droppers, once the solution flows through the tapered end and into the bulb, subsequent inversion will not return the solution to the cylinder. The sealing bulb should be deflated before slipping it over the open end of the assembly, thus creating a partial vacuum and preventing the bulbs from blowing off during autoclaving.

Fig. 1 (Elkin). A sterile unit for office use.

As a safety measure a thermostable preservative should be included in the solution. For convenient, dust-free storage these units can be sealed and autoclaved in individual envelopes.

Several of these units were prepared and tried under usual office conditions. They were found to be satisfactory. It is suggested, however, that care be exercised in opening these units to prevent splattering with the solution.

Sterility tests were conducted after one month's storage in the office. The preservative was inactivated by dilution, and incubation was carried out for one week at 37°C. In no case was any bacterial growth observed.

4033 Brockton Avenue.

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2. Bignell, J. L.: Infection of the cornea with B. pyocyaneus. Brit. J. Ophth., **35**:419, 1951.
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OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.

Abstracts of papers presented at the Ninth Annual Clinical Conference at the Wills Eye Hospital, Philadelphia, Pennsylvania, February 8 and 9, 1957

The Ridley operation: An interim report. Warren S. Reese, M.D., and Turgut N. Hamdi, M.D., Philadelphia.

This brief communication recounts our experiences with 113 cases in which we implanted an acrylic lens in the space from which we removed a cataractous lens. It is unfortunate that in this country few mature ophthalmic surgeons have attempted the Ridley operation so there is practically no literature on it and none, to my knowledge, on the modifications that have been proposed by various European ophthalmologists. On the other hand, we know of several cases in which the Ridley operation has been performed by men who should never have undertaken it, either because they were unskilled or had not prepared themselves properly.

When consulted by a patient who may be a prospective Ridley case, we discuss the situation frankly and tell him exactly what he can look forward to. If he has a unilateral cataract, we tell him that the Ridley operation is indicated, particularly if his work requires binocular vision. We explain that if the other eye should become cataractous, he would then require a Ridley operation on it also. If the patient has a bilateral cataract, we do not suggest the Ridley operation but agree to do it if he wishes. All patients are told that the Ridley operation is slightly more hazardous and that certain things may occur at time of operation to make us convert it into a conventional extraction. These are mainly loss of vitreous, undue dilatation of the pupil, and an unmanagable patient. We state that the main objection to this new method, foreign-body reaction, is theoretic and not based on fact, at least in our experience up to the present. We also admit that it is too early to evaluate the operation accurately.

Included in this series are a locomotive engineer, a commercial pilot, and a surgeon, all of whom were able to resume their occupations because of this operation. Traumatic cataracts and cataracts in young people are more difficult and do not offer as good prognosis.

Postoperative care is most important, often difficult, and, when neglected, may have serious results. We had one patient whose vision was practically gone when seen one year after operation. He had consulted a doctor in Florida who was so prejudiced against the Ridley operation that follow-up was discouraged. Probably the greatest danger is from a severe postoperative reaction. Complications are, if anything, less frequent than in conventional cases, particularly iris prolapse and anterior chamber hemorrhage.

The unilateral cataract case. Edmund B. Spaeth, M.D., Philadelphia.

The person with a cataract in one eye only has always been an unhappy person, because he is given the not uncommon advise, "wait for surgery until the other eye has become involved." While this advice has not been universal it still is not uncommon. This delay can result in much permanent visual impairment. Heretofore, the difficulty experienced in wearing a correcting lens after operation for unilateral cataract has prevented the satisfac-

tory use of such an operated eye. A series of over 100 such cases showed that single binocular vision can be restored after such an operation, without diplopia, through the use of a satisfactorily fitting contact lens. In this procedure two considerations are stressed: (1) early operation, and, (2) the use of a certain type of corneoscleral contact lens, carefully fitted by skilled technicians. From 80 to 90 percent of such cases can be handled in this manner with little difficulty and with very satisfactory results.

Evaluation of ocular signs and symptoms in myasthenia gravis. Nathan S. Schlezinger, M.D., and Walter A. Fairfax, M.D.

A series of 52 patients with myasthenia gravis has been observed at the Wills Eye Hospital within the past 16 years. The patients in this series are considered to be representative of the patients with myasthenia gravis who would be likely to present themselves to the ophthalmologist. The entire series has been surveyed with regard to age and sex incidence, mode of onset, course of illness and treatment.

Within a three-year period 16 patients were observed to have myasthenic involvement which remained limited to the eyes. This "ocular" group appears to have a relatively good prognosis in terms of life expectancy. The treatment of ocular myasthenia may include corticotropin therapy in selected instances when extraocular muscle pareses are relatively refractory to Neostigmine or Mestinon medication.

Novobiocin: A new antibiotic: Its ocular penetration and tolerance. Theodore W. Sery, Ph.D., S. D. Paul, M.D., and Irving H. Leopold, M.D., Philadelphia.

Novobiocin (trade names: Cathomycin, Albamycin, Cardelmycin, Streptonovicin) was administered to rabbits by several routes. Aqueous and vitreous withdrawn from different animals at regular intervals were subjected to a bio-assay procedure by making serial dilutions in nutrient broth and noting the growth inhibiting properties of the mixtures against a strain of Staph. aureus. The presence of 20 to 30 μg./ml. of the drug represented a relatively significant level for inhibition of sensitive bacteria.

Local application of a solution concentration of 10,000 μg./ml. did not lead to detectable amounts in the aqueous of normal eyes. In eyes with mechanically abraded epithelium, however, 20 to 30 μg./ml. was detected in the aqueous. Concentrations of 25,000 μg./ml. were toxic to the ocular tissues. Subconjunctival injections of 12,500 μg. led to significant amounts in the aqueous. Lower dosages were apparently inadequate and higher ones were toxic.

Intravenous injections of 500,000 μg. led to aqueous levels of 20 to 30 μg./ml. when serum levels measured around 240 μg./ml. Higher aqueous levels were found in animals that had received acid burns of the cornea. In these same animals the secondary aqueous taken 30 minutes later was found to contain three- to nine-fold increase in Novobiocin over that found in the primary aqueous. Generally the best aqueous level was reached during the second and third hour and was almost gone by the sixth hour. Intra-aqueous and vitreous injections of 2,000 μg. or less were well tolerated and were detectable in the vitreous after 24 hours.

Further studies of the use of radioactive isotopes for ocular diagnosis. Paul L. Carmichael, M.D., and Irving H. Leopold, M.D.

A total of 200 cases of suspected ocular malignancy was studied in the Wills Hospital isotope department from April, 1954, to December, 1956. Of these cases, 79

were studied pathologocially or had successful surgical results.

A total error of 15 percent in the performance of all tests was noted. This included those lesions inaccessible to the anterior probe. The accuracy of the test was better than 90 percent when the inaccessible lesions were not considered in the results.

It is suspected that iris lesions may not adhere to the original 30 percent criteria. In a total of 11 cases studied six lesions were pathologically proven. It was noted in all cases of malignant melanoma of the iris that a low initial uptake of P^{32} was found with a subsequent increase in the 24-hour count.

Tonography in infantile glaucoma. Leonard Apt, M.D.

Tonograms were performed on 23 infants and young children thought to have congenital glaucoma, to determine the usefulness of aqueous outflow studies in the diagnosis and management of the disease. Control values were obtained from tonograms performed on normal subjects three months to four years of age. The facility of aqueous outflow was measured, under general anesthesia (rectal pentothal), by the method described by Grant, using an electronic tonometer attached to a Leeds and Northrup recorder.

In the normal eyes, the ocular tension varied from 11 to 24 mm.Hg; the coefficient of aqueous outflow ranged from 0.15 to 0.31 cu.mm./min/mm.Hg pressure. Similar figures for the facility outflow have been reported in normal adults.

There was a good correlation between the reduction of the coefficient of aqueous outflow and the severity of the glaucoma state, as determined by clinical evaluation. This correlation was not as consistent when ocular tension and the disease were compared.

Tonography proved useful in (a) diagnosis of megalocornea unassociated with glaucoma, (b) establishing the diagnosis of congenital glaucoma in infants with mild symptoms and normal or equivocal ocular tensions, and (c) evaluation of the effectiveness of antiglaucoma surgery.

Since impaired aqueous outflow may not be manifest by an elevated ocular tension because of the elasticity of the outer coats of the infant's eye, tonography provided a more precise method for the determination of an obstructed outflow of aqueous humor, and in evaluating the status of glaucoma control with the therapy used.

Angulations of the bony orbital walls in horizontal strabismus. Arthur Hail Keeney, M.D., Louisville, Kentucky.

This is a radiographic study of the angulations of the bony orbital walls in special submento-vertex projection designed to (1) establish normal radiographic values for the angulations of the orbital walls in orthophoric individuals of different sex, age, and race, and (2) analyze such bony orbital angles in relation to nonaccommodative and, apparently, nonparalytic strabismus of the purely horizontal type. Findings in 134 individuals between the age of eight months and 33 years are reported.

The angle between the medial and lateral orbital wall on the indicated side is designated "1"; the angle formed by projecting posteriorly the lateral walls of each orbit is designated "3."

In 68 orthophoric control patients, right and left angles 1 are equal in 60 percent of whites and 50 percent of Negroes; remaining cases show inequalities averaging 1.5 degrees and ranging below 10 degrees. Angle 1 values are essentially the same in white and colored individuals below the age of 12 years, but older Negroes show larger values. All angles are slightly larger in males than in females. Angles 3 average 95 degrees (range 81 to 107 degrees) in the whites and 98 degrees (range

88 to 120 degrees) in Negroes. Medial orbital walls are parallel in 12 percent of cases, and usually converge or diverge by a few degrees.

Twenty-five percent of monocular esotropic patients show significantly smaller angle 1 values (differing by amounts of four to 21 degrees) on the side of the deviating eye. Only 22 percent of monocular estropes show equal angle 1 values, compared to 55 percent in the control series.

In alternating esotropia, no significant inequalities are found between right and left angles 1.

Thirty-three percent of monocular exotropic patients show significantly larger angle 1 values (differing by amounts of four to 11 degrees) on the side of the deviating eye. Only 13 percent of monocular exotropes show equal angle 1 values.

No significance is attached to the medial orbital walls.

The incidence of medial versus lateral deviation is markedly different in the races represented in this series. Among the 44 white patients with purely horizontal strabismus the ratio of exotropia to esotropia is one to three; among the 22 Negro patients it is five to six.

Observations on the implantation of solid substances into the lens in vivo. Adolph W. Vogel, M.D., Philadelphia.

A method developed in this laboratory of making pellets of various sizes has been utilized for in vitro studies of the passage of various dyes through the lens substance in the living rabbit eye, and the effect of implantation of several enzyme inhibitors —NaF and iodoacetic acid—on the clarity of the lens nucleus and cortex. Preliminary observations indicate that the speed of migration of the dye is roughly dependent on its molecular size. The enzyme inhibitors used cause opacities around the site of implantation. Preliminary measurements of the size, rate of spread, and disappearance of the opacities have been made.

My surgical management of lateral rectus paralysis. William E. Krewson, 3rd., M.D., Philadelphia.

The use of superior and inferior rectus tendon-transplantation operations in the surgical treatment of lateral rectus paralysis is discussed, with particular reference to modification of the Hummelsheim operation. A case is reported of traumatic, bilateral abducens paralysis, treated with bilateral transplantation surgery, resulting in binocular single vision with abduction. My technique is presented together with indications and contraindications for its use. Included is a review of the mechanism by which the operation accomplishes its purpose.

Experimental intracameral acrylic implants: A preliminary report. Samuel L. DeLong, M.D., Philadelphia.

A brief history is given of the work done with these lenses in human eyes and specifications of the lenses used in humans and animals are outlined.

Unsuccessful experiments were first performed on rabbits and cats. The present study outlines results in eight dog eyes, three of which were unsuccessful. The remaining five eyes quieted well and acrylic strips remained in good position. Anterior chambers were clear except for small fibrous tissue strands on or behind the acrylic strips in three eyes.

A few of the advantages of the Strampelli type lens as opposed to the Ridley lens are mentioned.

Measures to prevent the introduction of foreign bodies in intraocular surgery. Clemens Kirchgeorg, M.D., Neenah, Wisconsin.

A review of the literature indicates that lint, cotton fibrils, rubber, glass, gold, cilia, talc, and ointment may be introduced into the eye during surgery. Methods that will minimize this problem are:

Wash all linens with Migasol P. J.

(Ciba). Distill the water used for solutions. Sterilize distilled solutions by autoclaving and store in gallon jugs. Wipe pans and trays with sterile gauze before use. Cold-sterilize rubber goods, bottles, and cups. Inspect erisophakes with a slit-lamp after cleaning. Use plastic sponge wicks instead of cotton applicators to clean the operating field. Avoid irrigation of the anterior chamber by keeping a dry field during surgery. Shave eyebrows and trim lashes preoperatively. Avoid talc by not using gloves. Reduce air contamination with ultraviolet lamps. Remove particles from the air with an electronic air cleaner.

Ophthalmic Miniature

The third rule is, that it is always a matter of urgent necessity to preserve the eyes from a light too vivid.

For example, every hat or bonnet of any other colour than black, grey, blue or green, and particularly when the inside or lining is smooth and shining, ought to be considered as an article of the most pernicious quality; for in the same manner as water, or the snow in the streets, reflects the light by a thousand different rays, so does this brilliant lining throw it down upon the pupil, where it causes more ravages than even the direct rays of the sun itself upon the weakest eyesight.

. . . Yet it must be candidly acknowledged that cases may occur which will resist this remedy, particularly in high winds, during the heat of the Summer; for then no sooner does a person expose himself to their effects, than he feels a great dryness about the eyes, with some difficulty in opening and shutting them, and the eyelids suddenly become so red, that a degree of inflammation generally ensues. In such cases, cold water is not alone sufficient; but certain relief will always be found in the application of a simple lotion, in the proportion of four ounces of rose water (or quarter of a pint) with a drachm of gum arabic, and about fifteen drops of the acid of litharge of gold, or, in its stead, half a drachm of white vitriol, which may be further diluted if the eyes are very tender. Such a remedy is of easy carriage, and may be renewed as often as thought necessary at a very small expense.

H. Colburn, *The Art of Preserving the Sight Unimpaired to an Extreme Old Age*, London, 1816.

PROGRAM

of the

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

*26th Annual Meeting**

Tropical Room—Park Sheraton Hotel—New York City

June 3 through June 6, 1957

Monday, June 3, 1957

Beginning at 9:00 A.M.

EFFECTS OF TACHISTOSCOPIC TRAINING ON VISUAL FUNCTIONS IN MYOPIC PATIENTS
Conrad Berens, Louis J. Girard, Gerald Fonda, and Saul B. Sells

THE HUMAN OPTIC PAPILLA: A DEMONSTRATION OF NEW ANATOMIC AND PATHOLOGIC FINDINGS
J. Reimer Wolter

CONTINUING STUDIES ON THE ASSOCIATION OF ADENOVIRUS TYPE 8 WITH EPIDEMIC KERATOCONJUNCTIVITIS
L. Hanna, E. Jawetz, Y. Mistui, P. Thygeson, S. Kimura, and A. Nicholas

PRECIPITATING ANTIBODIES TO TOXOPLASMA: A FOLLOW-UP STUDY OF FINDINGS IN THE BLOOD AND AQUEOUS HUMOR
G. Richard O'Connor

FACTORS UNDERLYING THE DEVELOPMENT OF THE CILIARY PROCESSES
Alfred J. Coulombre and Jane L. Coulombre

THE EFFECTS OF MATERNAL HYPOXIA ON INHERITANCE OF RECESSIVE BLINDNESS IN MICE
Aeleta Nichols Barber

DISTRIBUTION OF RADIOACTIVE SULFATE IN THE DEVELOPING EYE
George K. Smelser and Victoria Ozanics

OXYGEN STUDIES IN RETROLENTAL FIBROPLASIA: VI. THE EFFECTS OF CONCENTRATION AND DURATION OF EXPOSURE TO OXYGEN ON EXPERIMENTAL OCULAR LESIONS
Arnall Patz

Beginning at 1:30 P.M.

THE RESPONSE PATHWAY FROM PHOTORECEPTOR TO NERVE CELLS IN THE LIMULUS LATERAL EYE
Leo E. Lipetz

STUDIES OF PHOTORECEPTOR STRUCTURES
Jerome J. Wolken

ELECTROMYOGRAPHY OF FUSIONAL MOVEMENTS
Frederick C. Blodi and Maurice van Allen

AUTONOMIC INNERVATION OF EXTRAOCULAR EYE MUSCLES
Walter Mitchell and Gerhard A. Brecher

THE EFECT OF ULTRASONIC RADIATION UPON THE RATE OF ABSORPTION OF BLOOD FROM THE VITREOUS
Gilbert Baum

OCULAR EFFECTS OF SYSTEMIC SIDEROSIS
Paul A. Cibis, E. Brown, and S. M. Hong

CYTOCHEMICAL AND MORPHOLOGIC CHANGES IN CORNEAL STROMAL CELLS FOLLOWING WOUNDING
Virginia L. Weimar

FURTHER STUDIES ON THE VIABILITY OF FROZEN CORNEAS: AS DETERMINED IN TISSUE CULTURE
Jerry W. Draheim, Samuel D. McPherson, Jr., Virginia J. Evans, and Wilton R. Earle

STUDIES OF BRUCH'S MEMBRANE: I. RESULTS OF FLOW STUDIES THROUGH A BRUCH'S MEMBRANE-CHOROID PREPARATION
Wood Lyda, Nils Eriksen, and Narendra Krishna

Tuesday June 4, 1957

Beginning at 1:30 P.M.

A STUDY OF THE UPTAKE OF P^{32}, Zn^{65} AND I^{131} BY EXPERIMENTAL MALIGNANT MELANOMA
James F. O'Rourke, Humphrey Patton, and Robert Bradley

ANTERIOR CHAMBER PERFUSION STUDIES: II. CONTROLLED PARTICLE SIZE IN RELATIONSHIP TO PORE SIZE
Philip A. Peter, Wood Lyda, and Narendra Krishna

A STUDY OF THE INNERVATION OF THE CHAMBER ANGLE: PART II. THE ORIGIN OF TRABECULAR AXONS REVEALED BY DEGENERATION STUDIES
Monte G. Holland, Ludwig von Sallmann, and Eleanor M. Collins

THE EFFECT OF SUCCINYLCHOLINE ON THE EXTRAOCULAR STRIATE MUSCLES AND ON THE INTRAOCULAR PRESSURE
F. J. Macri

ON THE OCCURRENCE OF PROTEOLYTIC ENZYMES IN NORMAL AND CATARACTOUS LENSES
E. Albert Zeller and Anima Devi

THE TRANSCORNEAL POTENTIAL
Albert M. Potts and Robert Modrell

* Annual Banquet—Wednesday, June 5, 1957, Baroque Room, Belmont Plaza Hotel, 7:00 P.M.

INCORPORATION OF S^{35}-INORGANIC SULFATE INTO MUCOPOLYSACCHARIDES OF CORNEA
Bernard Wortman and Jack L. Strominger

FRIEDENWALD MEMORIAL LECTURE

Wednesday, June 5, 1957
Beginning at 1:30 P.M.

IN VIVO INTRALENTRICULAR IMPLANTATION OF VARIOUS DYES AND ENZYME INHIBITORS
Adolph W. Vogel

IN VITRO LENS STUDIES: II. PRODUCTION OF CATARACTOUS CHANGES
Marguerite A. Constant

STUDIES ON THE CRYSTALLINE LENS: VIII. ASCORBIC ACID AND MITOTIC ACTIVITY IN CULTURED LENSES
V. Everett Kinsey

STUDIES ON THE SULFHYDRYL GROUPS OF LENS
Lorenzo O. Merola and Jin H. Kinoshita

BUSINESS MEETING

STUDIES ON PROTEIN AND PROTEIN SYNTHESIS OF THE LENS IN GALACTOSE CATARACT
Zacharias Dische, Joshua Youlus, and Ginevra Zelmenis

INSULIN AND THE LENS
T. Farkas and John W. Patterson

LENS PROTEINS
Jules François

LENS PROTEINS
Robert A. Resnik

Thursday, June 6, 1957
Beginning at 1:30 P.M.

SOLUTION OF THE DIFFERENTIAL EQUATIONS PERTAINING TO AQUEOUS HUMOR DYNAMICS
Samuel I. Askovitz

THE EFFECTS OF GANGLIONIC BLOCKING BLOOD ON AQUEOUS FLOW IN NORMAL AND GLAUCOMATOUS SUBJECTS
David A. Rosen

THE AQUEOUS: PLASMA STEADY-STATE RATIOS OF POTASSIUM AND SODIUM AND THE INFLUENCE OF DIAMOX AND DIBENAMINE THERCON
John E. Harris, A. Eugene Carlson, Louise Gruber, and Gertrude Hoskinson

STUDIES ON THE MODE OF ACTION OF PILOCARPINE ON AQUEOUS OUTFLOW: CORRELATION OF TONOGRAPHIC AND GONIOSCOPIC DATA WITH HISTOLOGIC STUDIES OF THE TRABECULAR MESHWORK OF MONKEY EYES
Milton Flocks and H. Christian Zweng

DYNAMICS OF DIAMOX-INDUCED BICARBONATE CHANGES IN AQUEOUS HUMOR OF RABBIT EYE
Harry Green, Mayer J. Mann, Samuel I. Askovitz, and Irving H. Leopold

THE BICARBONATE CONCENTRATION OF GUINEA PIG AQUEOUS HUMOR: EFFECT OF SCURVY AND OF ACETAZOLAMIDE
Bernard Becker

THE TRITIUM STEADY-STATE OF THE RABBIT EYE
Frank W. Newell

PROCTOR MEDAL RECIPIENT LECTURE

PROGRAM

of the

SECTION ON OPHTHALMOLOGY

American Medical Association

New York City

Wednesday morning, June 5, 1957; Thursday morning, June 6, 1957;
Friday morning, June 7, 1957

9:00 A.M. to 12:00 M.

Wednesday, June 5, 1957

CHAIRMAN'S ADDRESS: THE DIFFERENTIAL DIAGNOSIS OF MELANOMA OF THE UVEA FROM SIMULATING LESIONS
A. B. Reese, New York

ADDRESS OF INVITED FOREIGN GUEST: THE DIFFERENTIAL DIAGNOSIS OF THE TAPETO-RETINAL DEGENERATIONS
Prof. J. François, Ghent, Belgium

OCULAR INVOLVEMENT IN NEVOXANTHO-ENDOTHELIOMA: REPORT OF TWO CASES
Frank W. Newell, Chicago
Discussion to be opened by T. E. Sanders, Saint Louis

PARS PLANA CYSTS
Samuel T. Adams, Montreal, Quebec
Discussion to be opened by Herbert M. Katzin, New York

IMPROVEMENT IN THE HYPERTENSIVE RETINOPATHY OF 109 PATIENTS FOLLOWING COMBINED ADRENAL RESECTION AND SYMPATHECTOMY
William C. Frayer, Philadelphia
Discussion to be opened by John Wendland, Minneapolis

MALIGNANT MELANOMA OF UVEA: OBSERVATIONS ON GROWTH AND BEHAVIOR: ENUCLEATION REFUSED OR LONG DELAYED
Banks Anderson, Durham, North Carolina
Discussion to be opened by Lorenz Zimmerman, Washington, D.C.

STUDIES ON CONTINUOUS ELECTROCARDIOGRAPHY DURING OCULAR SURGERY
Ralph E. Kirsch, Philip Samet, and Victor Kugel, Miami, Florida
Discussion to be opened by Harold F. Falls, Ann Arbor, Michigan

Thursday, June 6, 1957

EXECUTIVE SESSION

ADDRESS OF INVITED FOREIGN GUEST: IRIDENCLEISIS IN BUPHTHALMOS
Frank W. Law, London

EVALUATION OF NEW ANTICHOLINESTERASE AGENTS IN GLAUCOMA
Irving H. Leopold, David Gold, and Paul Gold, Philadelphia
Discussion to be opened by H. Saul Sugar, Detroit

A SURGICAL APPROACH TO TOTAL XEROPHTHALMIA THROUGH TRANSPLANTATION OF THE PAROTID DUCT
James E. Bennett and Arby L. Bailey, Cleveland
Discussion to be opened by Trygve Gundersen, Boston

NEW ASPECTS OF OPHTHALMONEUROLOGIC DIAGNOSIS
Goodwin M. Breinin, New York
Discussion to be opened by Francis Heed Adler, Philadelphia

Friday, June 7, 1957

SYMPOSIUM ON PROBLEMS IN CATARACT EXTRACTION

FIVE YEAR'S EXPERIENCE WITH THE RIDLEY OPERATION
Warren Reese and Turgut Hamdi, Philadelphia

ACRYLIC LENSES IN THE ANTERIOR CHAMBER: EXPERIMENTAL STUDIES IN ANIMALS
J. H. King, Jr., and Raymond Skeehan, Washington, D.C.

CLINICAL REPORT ON THREE CASES OF POSTOPERATIVE EPITHELIAL DOWNGROWTH TREATED BY CURETTAGE AND CAUTERY WITH 70 PERCENT ALCOHOL
John C. Long and George S. Tyner, Denver

CATARACT EXTRACTION AND AQUEOUS OUTFLOW
James E. Miller, G. Richard Keskey, and Bernard Becker, Saint Louis

TONOGRAPHIC AND GONIOSCOPIC STUDIES BEFORE AND AFTER CATARACT EXTRACTION
Pei-Fei Lee and Robert R. Trotter, Boston

CONTACT LENSES IN APHAKIA
Everett L. Goar, Houston

COMPARISON OF THE PERIPHERAL IRIDECTOMY VS. THE KEYHOLE IRIDECTOMY
David S. Johnson and Ralph Pino, Detroit

CONSERVATISM IN THE TREATMENT OF CONGENITAL CATARACT
Frank D. Costenbader, Washington, D.C.
Discussion to be opened by John Dunnington, New York; Peter Kronfeld, Chicago; John McLean, New York; A. Edward Maumenee, Baltimore, and Derrick Vail, Chicago

OPHTHALMIC MINIATURE

But the scientist requires, besides the information which lectures and books send out to him, also in addition knowledge which can be given only by an abundant and attentive sensitive observation. He requires skills which are obtainable only by often repeated experiments and long practice. His senses must be sharpened for certain kinds of observation, for slight variations in form, color, hardness, odor, etc. of the examined objects. His hand must be practiced to execute now the work of a smith, of a mechanic, of a carpenter, now that of a draughtsman or violinist and, now, when he dissects under the microscope, to excell in precision that of the lacemaker's needle.

Hermann von Helmholtz,
From the address, *The Objective and the Progress of Natural Science*,
Delivered, 1869, at Innsbruck.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

CHICAGO OPHTHALMOLOGICAL SOCIETY

October 1, 1956

DR. KENNETH L. ROPER, *President*

CLINICAL PROGRAM

(Presented by Department of Ophthalmology, Northwestern University)

PTOSIS AND VERTICAL MUSCLE ANOMALIES

DR. WARREN BINION presented a nine-year-old child who had a bilateral ptosis and a marked right hypertropia. The primary extraocular muscle defect was a double elevator paresis in the left eye with a corresponding overshoot of both elevators in the right eye. It was decided to correct the vertical anomaly first, and therefore, on September 7, 1956, a recession of the right superior rectus and of the right inferior oblique was performed. Postoperative appearance showed a marked improvement in the ptosis as well as in the right hypertropia.

Discussion. DR. BEULAH CUSHMAN: This is an interesting patient because of her bilateral congenital ptosis and her rather marked blepharophimosis. When we find levator paresis we feel it is necessary to correct that before taking care of any ptosis. She had a paresis of both levators of the left eye, and they were taken care of and her ptosis is already improved a great deal. She has the beginning of a fold in the right lid, as well as a very small one in the left. We'll watch her now for six months and then any resulting ptosis will be taken care of by a Blaskovicz operation. But she has, if you will notice, very narrow lids so she may not be able to have a ptosis operation, and with the change that we get with the elevation as it is now, I hope she will not need it.

The reason that we present this case is that we feel it is most important to correct a vertical muscle anomaly before correcting a ptosis of the lid.

SCIENTIFIC MEETING

BILATERAL METASTATIC CARCINOMA TO CHOROID AND OPTIC NERVES

DR. STEFAN VAN WIEN and DR. DAVID SHOCH presented an unusual case of metastasis of a breast carcinoma to the choroid and optic nerves of both eyes resulting in massive retinal detachments. The eye findings preceded the definitive diagnosis of a malignancy of the breast by eight months.

RECENTLY RECOGNIZED CAUSE OF BUPHTHALMOS

DR. FRANK NEWELL gave a preliminary report on a case of buphthalmos caused by a local nevoxantho-endothelioma. The associated systemic findings were reviewed, as well as the ocular pathology.

Discussion. DR. GEORGIANA THEOBALD: It is very difficult to know what to say after Dr. Newell did such a nice job of reporting these two cases.

The second case that he reported I examined with Dr. Bothmann years and years ago when the eye came through the clinic. We didn't know what the tumor was exactly, but we did know that it wasn't a melanoma or one of the ordinary tumors that arise in the iris.

It is difficult to place the pathology of these tumors. They either have cells in them that look exactly like malignant tumor cells, and then you have other cells which belong to the reticulo-endothelial system that are inflammatory cells. I don't think that one would want to keep an eye like this in the head, even though the child had xanthoma lesions all over his body, because it might lead to more serious complications.

The second eye was more easily diagnosed than the first one because it had been of shorter duration. I think that we are very fortunate that buphthalmos does not occur more frequently than it does, and since these cases have been reported I have gone over the records at the Eye and Ear Infirmary, and I know that in the past 50 years we haven't had a single case of this kind of tumor.

DR. JOSEPH S. HAAS: I had the privilege of reading Dr. Newell's very excellent paper prior to this evening's meeting. There are several things that interest me very much about it from a clinical standpoint.

First, I don't believe that I have ever, at least to the best of my knowledge, recognized a case of this type, although I have been aware of the existence of this condition since 1954 because, prior to the Panel on Congenital Glaucoma at the American Academy, Dr. Sanders presented a clinical pathologic case presentation of nevoxantho-endothelioma. It was a classical case.

I was very much relieved to hear Dr. Theobald say that she hadn't seen one at the Infirmary either because it may mean that we haven't missed too many of them. Clinically, however, I think it may be important to point out that this is a secondary glaucoma. It is distinct from the primary type of infantile glaucoma in which there is no infiltrate of the trabecula, and, being a secondary type of glaucoma, I think it should be pointed out that the glaucoma most likely occurs as a result of the infiltration of the trabecula and canal of Schlemm by the cells that are found in these cases. I think that goniotomy is unsuccessful in these cases because the surgeon is cutting a mass of infiltrated granulation tissues. And characteristically, as the disease regresses, one would assume that there would develop an atrophic type of scar, such as develops in the skin, and, therefore, it seems reasonable that goniotomy should not succeed even after the active phase of the disease has passed because of the altered trabecula.

This brings me to the final clinical point and one that surprises me a great deal. Dr. Newell's case is the first case that has responded to antiglaucomatous therapy and then gone on to produce a useful eye.

It is surprising in a disease in which hemorrhage is a very paramount factor that this eye could withstand trephining and not bleed. I should like to ask Dr. Newell if the reason that his case did not bleed might be due to the fact that eight months elapsed between the onset of the disease and the therapeutic trephination, permitting the active phase of this disease to subside to the point that trephining could safely be done on this eye.

If this follows, then it would be well to attempt to treat conservatively many of these cases until the time at which the active phase of the inflammation had subsided and antiglaucomatous filtering operations could safely be done. I should like to thank Dr. Newell again for pointing out this condition which is probably one of the very few conditions, if not the only condition, which causes unexplained spontaneous hemorrhages in the anterior chamber in infants and causes buphthalmos of a secondary nature.

DR. NEWELL: I want to thank Dr. Theobald and Dr. Haas for their generous remarks.

I'd like to emphasize that the first patient did not present skin lesions, and this apparently was a visceral involvement only. Dr. Bothmann, who managed this case, I think deserves much, much credit for his ingenuity in doing an anterior-chamber paracentesis, and finding these cells. They were diagnosed as retinal nuclear layer cells which certainly, with the marked variation in cells that histiocytes might assume, is understandable.

Dr. Haas has correctly emphasized that this is a secondary type of glaucoma and I agree that we should not be too sanguine about having salvaged this single eye. It may well have been a coincidence.

We were pleased, however, at getting from the iris, characteristic changes and in escaping without destroying the eye through hemorrhage. The skin lesions as yet have not disappeared, and the child is now nearly two. The iris, however, appears normal, and it may well be that our surgery was coincident with the spontaneous regression.

Topical use of isopropylnoradrenalin

Dr. Robert H. Monninger (by invitation) presented a clinical study on the use of isopropylnoradrenalin (isopropylarterenol, Isuprel®) in glaucoma. He stated that this drug is an analogue of epinephrine and causes a reduction of ocular tension when applied locally. In a series of 10 cases the 0.5-percent solution was found to be tolerable while the one-percent preparation caused much irritation. The range of reduction in tension in these 10 cases was 5.0 to 13 mm. Hg. Apparently the mechanism of action is by reduction in formation of aqueous. Therefore, in those cases with an interference in the outflow mechanism, a local miotic must be used in addition to the Isuprel®. Dr. Monninger felt that the combined effect of these two agents is superior to the combined effect of a miotic and Diamox®.

Discussion. Dr. Julia Apter: One reason that the drug presented here tonight seems like a new secret weapon is that the name on the program, isopropylnoradrenalin, is probably the least frequently ascribed to it. The others that Dr. Monninger told you about are much more common than this actually correct chemical name. I did know about Isuprel® but had not used it because I believed the reports that the tachycardia was difficult for the patients to endure. But, in Weekers' article, which Dr. Lebensohn so beautifully translated for The American Journal of Ophthalmology, and therefore made so easy for me to read, they were especially interested in this drug because they thought it might be applicable to narrow-angle glaucoma as well as to wide-angle glaucoma because it was a sympathomimetic drug that did not dilate the pupil. They came to the conclusion from the study of epinephrine and epinephrinelike drugs that these drugs do not all reduce the tension. However, they do not seem to realize that were they to look at their records the way we looked at Diamox® records when they were first published, they would find they do not reduce the tension in normal eyes but they all reduce the tension in glaucomatous eyes.

I wish I had the article here to show you how striking it is that up to tension of 28 all of the epinephrine drugs do not reduce tension. But d-epinephrine and arterenol will reduce the tension even though they are not as strong in reducing the production of aqueous as isopropylnoradrenalin and l-adrenalin. But, they will all reduce the tension in glaucomatous eyes.

It was so striking that it seemed to me that it was possible to use this particular sign as an indication as to whether a tension of 28 is in a normal eye or in a glaucomatous eye.

I was delighted to hear that in the particular series of cases presented tonight there was no debilitating tachycardia although apparently there was some that was measurable. I can't help but point out to you—perhaps many of you know what I have been trying to say—that sympathetic innervation of the muscle does not dilate the pupil, and that we have come to this conclusion mainly upon the basis of the observation of the actions of these drugs. That actually these drugs are all vasoconstrictors and that is why they dilate the pupil.

Isopropylnoradrenalin is a beautiful example in point. It is one sympathomimetic drug that does not dilate a pupil, and I would ask that we all keep in mind the fact that this is one drug that reduces the production of aqueous and also does not dilate the pupil, therefore, it should be investigated for possible use in narrow-angle glaucoma as well as wide-angle glaucoma.

DR. JAMES E. LEBENSOHN: Several have asked me whether Isuprel® is on the market. It is very much on the market and we used, for the most part, the drug that was commercially available. It is used by inhalation for asthma and is one of the most popular drugs now for this purpose. It is also used underneath the tongue, but there it is apt to cause a tachycardia. In fact, this drug resembles adrenalin in some respects. It is more active than adrenalin in certain respects, while less active in mydriasis and vasoconstriction. In fact it is not a vasoconstrictor at all, nor a vasodilator.

It acts on the cardio-excitor mechanism much more than adrenalin and consequently has been used to stimulate cardiac action when you fear a cardiac arrest. That is a good point to remember. It could be placed or given under the tongue in cases where cardiac arrest has ensued during anesthesia.

Now I certainly want to thank Dr. Apter for a very thoughtful discussion, and the interesting observation that dextro-epinephrine did cause a reduction in the tension. I hadn't noted it myself because I took Professor Weekers' word that it had no noticeable effect, and I didn't study the data very carefully.

I would think that Isuprel® is probably contraindicated in narrow-angle glaucoma because I found that being a vasodilator it causes an increase of tension in practically all congestive conditions that are associated with the eye, so that I would very much hesitate to use it in narrow-angle glaucoma unless it was of a noncongested type or when there is no longer any congestion present. But, I certainly would not use it in acute glaucoma in which there is any evidence of activity—I mean as regards congestion.

I don't believe that the findings as regards Isuprel® can be extended to the action of levo-adrenalin to explain the mechanism of sympathetic action on the eye because there is a difference between the two drugs. It has been remarked that the sympathomimetic drugs have alpha and beta activities, that is excitatory and inhibitory, and they would vary with the different compounds. They have been classified along that line.

The question was asked whether the drug has any effect on the ocular tension when taken by mouth. I shouldn't think so. Its particular action would then be on the bronchi and on the heart. However, we have not investigated this point.

David Shoch,
Corresponding Secretary.

LOS ANGELES COUNTY MEDICAL ASSOCIATION

SECTION OF OPHTHALMOLOGY

May 3, 1956

NEW APPROACH TO SENILE MACULAR DEGENERATION

DR. SOL ROME reported on 23 cases of senile macular degeneration treated with intravenous heparin. One hundred mg. of concentrated aqueous heparin were given twice weekly, with a three weeks' rest period after each series of 10 to 20 injections.

The results were: nine cases showed marked improvement, with final visual acuity better than 20/40; four showed moderate improvement, with visual acuity after treatment between 20/70 and 20/40; four were slightly improved, with a gain of less than one line; three cases remained stationary; and in three visual acuity continued to diminish.

The speaker presented several cases in detail, with accompanying fundus photographs. The first patient discussed had bilateral colloid macular degeneration with superimposed disciform macular degeneration and definite pigmentary degenerative changes. Treatment with heparin was started in March, 1952. Vision before treatment was: O.D., 20/70; O.S., 20/100−1. A total of 120 injections was given over a three and one-half year period. Final visual acuity in September, 1955, was: O.D.,

20/25+2; O.S., 20/25−3. Color slides of the fundi before and after treatment showed disappearance of disciform lesions and pigmentation, and a definite reduction in the number of colloid bodies in the central area.

Another case with a fairly recent disciform macular lesion was presented. In the course of several months of the usual therapy, which included oral cortisone, vision had diminished from 20/30 to 20/60−3. After 20 injections of intravenous heparin, visual acuity improved to 20/25. Color slides of the fundus before and after heparin therapy were shown. Marked diminution of the size of the lesion and disappearance of the edema were evident.

A further series of slides was shown, in which 45 injections of intravenous heparin over an eight-month period resulted in absorption of established circinate changes surrounding a disciform macular lesion, and improvement of the lesion itself; in this patient vision returned from 20/100 to 20/60. In two other cases uncomplicated unilateral intracapsular cataract extraction was followed by gradual diminution of visual acuity in the operated eye, due to early disciform macular changes. In the first one of these cases, 35 injections of intravenous heparin were given over a four-month period, with vision improving from 20/200 to 20/25; in the second case, 30 injections over a six-month period improved vision from 20/60−3 to 20/30−3.

One case of beginning incomplete retinal hole in the macula was presented, with vision reduced to less than 20/200; 25 injections of heparin caused a marked diminution in the size of the cyst, with an improvement of vision to 20/25.

It was emphasized that early disciform macular lesions, in the stage of edema and exudation, before scar formation had taken place, showed by far the best response. Of 12 cases with disciform macular degeneration six were markedly improved, and three moderately improved. Of 10 cases with senile arteriosclerotic macular degeneration (Haab) two showed marked improvement, and one moderate improvement.

It was stressed that no untoward reactions were encountered in over 1,000 intravenous injections of heparin. The cases in this series were seen and treated in a routine office practice. Many of the patients were of advanced age, with hypertension and cardiovascular-renal disease. A hemorrhagic diathesis and active ulceration were listed as contraindications. Bleeding and clotting time controls were not done, because the anticoagulant effect of this dose of intravenous heparin is less than 12 hours. Protamine sulfate was kept on hand as a safeguard, but no occasion arose for its use. Patients were cautioned against bruising and cutting themselves as well as against minor surgery on the day of injection.

Discussion. DR. HYMAN ENGELBERG (by invitation) opened the discussion with remarks on the biochemical aspects of heparin and the current clinical and experimental investigations concerning the role of heparin in lipoprotein metabolism. He stated that the lipemia-clearing effect of heparin has been shown by Gofman and his co-workers to be due to the physiologic breakdown of lipoprotein molecules from larger to smaller sizes. One of the present concepts of the genesis of atherosclerosis is that it is initiated by entrapment of the larger lipoprotein molecules in the interstices of the walls of the arterial intima. He suggested that reduction of the size of these lipoprotein molecules may prevent one phase in this development, and may also prevent the formation of lipoprotein films and sludges which coat the intimal surfaces and interfere with normal metabolic interchange. He mentioned that some patients may have had a heparin deficiency prior to treatment, since it was demonstrated that subjects with coronary atherosclerosis have reduced heparin levels during life, and present a lower number of mast cells at autopsy. These mast cells are known to constitute the main source of endogenous heparin.

Chronic macular edema

Dr. Richard Kratz reported a case of chronic macular edema in a 35-year-old man, in whom vision could not be improved beyond 20/70, despite six months of therapy with vasodilators, steroids, and so forth. At the suggestion of Dr. Rome he gave 10 injections of intravenous heparin with improvement of vision to 20/20 at the end of this treatment, and almost complete disappearance of macular changes.

In the discussion the question was raised as to how long the improvement in visual acuity was maintained after cessation of therapy. Dr. Rome stated that to date no case has shown visual loss reverting to the pretreatment level; in several instances the vision diminished, but was brought back in all but one case to its original peak by additional treatment with heparin.

Richard P. Kratz,
Secretary, Eye Section.

MADRID OPHTHALMOLOGICAL SOCIETY

May 25, 1956

Dr. Marin Amat and Dr. Valentin Gamaza, *presiding*

Corneoscleral suture

Dr. Aguilar Muñoz presented a paper on "A continuous corneoscleral suture in cataract surgery."

This type of suture was used in 105 cases, proving to be beneficial and allowing an easy removal of the suture postoperatively in one or at most in two steps. A loop is placed at the end of the silk suture in order to fix its terminal end. The needle first passes through the anterior part of the cornea at one end of the incision, and is carried from the central to the peripheral border of the incision, making sure that the needle does not take a bite of more than half the depth of the cornea or sclera. The suture is carried in a continuous manner from one end to the other of the incision.

The section is made in cornea thus preventing bleeding into the anterior chamber. The closure guards against iris or vitreous prolapse and aids in the rapid formation of the anterior chamber (chamber is always present on the first dressing four days after surgery). In 105 cases of cataract surgery, using the continuous corneoscleral suture:

Hemorrhages in anterior chamber	0
Iris prolapse (no iridectomy or iridotomy had been performed)	2
Anterior chamber reformed on fourth day	105
Pupillary displacements in (21 vitreous hemorrhages)	0
Suture extracted	
at one sitting	82
at two sittings	23

Discussion. Dr. Marin Amat: I prefer to follow our technique established in 1914 of a U-corneo-scleral previously placed suture, with a limbal incision with the Graefe knife and total iridectomy.

I believe a continuous preplaced suture would encumber the extraction of the cataract and, if placed after extraction, may facilitate vitreous prolapse.

As to the purpose of simplifying the extraction of sutures after surgery, I have had no difficulty with my technique.

Dr. Aguilar Muñoz: The suture is firm and we have confirmed at the end of the operation that by pulling on the suture it will not come out but may deform the eyeball. Also, in 23 cases, we have had to cut the suture in half to take it out postsurgically. I find this suture easier to remove compared to other corneoscleral sutures, besides having the other benefits enumerated.

I have no difficulty with tangling with the following technique: corneal incision with keratome and Wescott scissors, placing a previous suture at the 12-o'clock position, iridectomy and extraction of the cataract, closing of the suture, and cutting the 12-o'clock previously placed suture when I reach it with the continuous suture.

We are happy with the results obtained

in the 105 cases in which we used this type of suture, and especially in the 21 vitreous hemorrhages where hermetic closure avoided further complications.

Simulated unilateral amaurosis

Dr. Marin Amat presented two cases. The first was that of an industrial worker, aged 58 years, who received an injury to his left eye while working and complained of loss of vision in that eye. On external examination, the eye was normal with good pupillary reflexes. The fundus was normal. The vision of the left eye was nil according to the patient but, with the appropriate means, the pretended blind eye had 20/20 vision and J1 for near.

The second case was that of a child, aged eight years, who was brought for consultation because of loss of vision of the left eye. On examination the right eye had normal vision, and the left eye none. External examination showed that the pupillary reflexes, fundus, and refraction were normal. Presently the simulation of visual loss was discovered and vision found to be normal.

Dr. Amat presented the differential diagnosis between true and false amaurosis in its two variations, hysterical and simulated and outlined his criteria for dealing with neuropathic patients and simulators; frequently both factors may be associated. A third variation appears when a slight ocular trauma is also present.

Sharpening corneal needles

Dr. Santalices Muñiz exhibited a type of needle with a characteristically straight, short, inferiorly sharpened border, triangular in section and with the rest of the needle flat inferiorly. The back is ovoid and more marked inferiorly; this allows the needle, at the moment of coming out, to follow its own curvature smoothly and without resistance.

The straight instead of the convex edge permits the needle to penetrate tangentially without tearing. The available needle models have a convex border and the surgeon is obliged to penetrate vertically in order to avoid complications.

Discussion. Dr. Garcia Castellon: We have been using lately the Grieshaber needles modified by Santalices. After having tried the new Santalices needle, I find that I can take in one bite the corneal and the scleral punctures.

Olga Ferrer,
Translator.

Ophthalmic Miniature

"This is a very singular knife," said Holmes, lifting it up and examining it minutely. "I presume, as I see blood stains upon it, that it is the one which was found in the dead man's grasp. Watson, this knife is surely in your line?"

"It is what we call a cataract knife," said I.

"I thought so. A very delicate blade devised for very delicate work. A strange thing for a man to carry with him upon a rough expedition, especially as it would not shut in his pocket."

Silver Blaze: The Memoirs of Sherlock Holmes.

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UVEITIS STUDY

The Uveitis Clinic at the University of California School of Medicine, Department of Ophthalmology, and Francis I. Proctor Foundation has been conducting intensive studies on patients with uveitis and in the laboratory to determine the etiology of this group of conditions.

At the present time investigations are directed toward the recovery of viral or other agents from such eyes. It is hoped that such viruses as may be present may be "unmasked" in a manner similar to that accomplished recently with the APC viruses. In order to carry out these studies fresh tissue is necessary, and the investigators hope to receive eyes for cultural studies as quickly as possible.

THE JOURNAL heartily recommends this project and hopes that all ophthalmologists

will co-operate by referring such tissues.

Derrick Vail.

DANGERS OF CORTICOTROPHIN*

It is well known that corticotrophin (ACTH), by stimulating the adrenal cortex, has a favorable action in allergic conditions. When this was first recognized there were fears that the widespread use of the hormone might be dangerous, not only because of the pharmacologic effects of impurities but also because sensitivity to the hormone, a foreign protein, might be induced. This fear was based partly on theoretic considerations, partly on previous experience with pituitary extracts, and partly on some experimental findings which suggested that guinea pigs sensitized to horse-serum and treated with corticotrophin to prevent anaphylactic reactions become sensitized to the corticotrophin itself.[1] Early clinical experience did not bear out these fears,[2] but gradually it became clear that corticotrophin did in fact occasionally produce symptoms that were unmistakably allergic, ranging from slight urticaria to severe collapse.[3-5]

In a series of 208 patients, Brown and Hollander[4] estimated the incidence of these manifestations at about three percent, and they pointed out that a similar incidence of allergy could be expected from the therapeutic use of insulin or liver extracts. When patients were hypersensitive to the hormone, Brown and Hollander recommended the substitution of beef corticotrophin for the more easily available and widely used hormone derived from the pig. But one of their patients later developed a positive skin reaction to beef corticotrophin as well. Thorn et al.[5] considered that reactions to corticotrophin were produced by "inert protein rather than by ACTH itself" (in their opinion the incidence had decreased with the increasing purification of the hormone); but it is interesting to note that Feinberg et al.[1] reported a strongly positive skin reaction to a "sheep corticotrophin peptide" in a sensitive subject. Thorn et al. make an important point when they say that patients with adrenocortical insufficiency are particularly liable to react adversely to corticotrophin; but here again it must be noted that in the case recorded by Feinberg et al.[1] there was a severe reaction to corticotrophin despite preceding treatment with cortisone for 12 days.

At least three cases have been described[6-8] in which the administration of corticotrophin was followed by death; and these disasters should be studied carefully by every clinician who decides on treatment with corticotrophin in preference to cortisone or its related compounds. The age of the patients ranged from 17 to 27 years; two were treated for asthma[6,8] and one for exudative dermatitis.[7] An initially good response to corticotrophin was followed by a relapse which led to the resumption of treatment after an interval of varying length. All three patients died during the second course of treatment. In the two asthmatics an injection of corticotrophin was followed almost immediately by collapse and death. The patients described by Hill and Swinburn[7] survived for about eight days. There was no clear-cut personal or family history of allergy, but in the patient with exudative dermatitis sensitivity to streptomycin ointment developed during the course of the illness. Unhappily, corticotrophin was given in one instance for a "moderately severe" attack of asthma; and the other two patients showed what in retrospect seem to be definite signs of sensitivity to corticotrophin. A negative skin test,[6] combined, presumably, with the then prevailing optimism about reactions to corticotrophin, encouraged the continued use of the hormone. It is of interest that in one case[7] the corticotrophin used for the challenging dose was derived from an animal different from that used for corticotrophin in the sensitizing course.

Eisalo et al.[8] say that at present it is impossible to decide whether the ill effects were

* Reprinted by permission from *The Lancet*, September 29, 1956.

caused by the hormone itself or by some other substance present in the preparation. But they raise the important question whether the indications for the administration of corticotrophin should not be reconsidered, since in most cases some of the more potent adrenocortical steroids can be used with advantage. It may be argued that the use of corticotrophin is more "physiological" and that we have to learn "to co-operate with the patients' adrenals"; but for most conditions hydrocortisone or related compounds will usually be adequate. Perhaps the best antidote for a reaction to corticotrophin, if time permits, is hydrocortisone or cortisone itself. Wilson's patient[3] recovered from a severe illness after being treated with adrenocortical extract, among other things.

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CORRESPONDENCE

SURGICAL CERTIFICATION*

Editor,

American Journal of Ophthalmology:

I read with interest the announcement of the formation of a Board of Ophthalmic Surgery by one, Merrill J. King.

As a diplomate of the American Board of Ophthalmology, I cannot recall being polled on the advisability of such a move. This is distressing, because for several months I have been in process of organizing a new board known as the "American Board of Ophthalmic Surgeons of the Right Eye." Very probably we can resolve our minor differences and merge the two boards, thus avoiding duplication of effort.

Everyone is aware that ophthalmology is far too broad a specialty. Since surgery was divorced from barbers (and to some extent, barbarism), EENT from surgery, and ophthalmology from EENT, we have been aware that our specialty is so broad we cannot devote the time to develop the niceties of hip and wrist motion that distinguish the true right eye surgeon. Naturally, it is the right eye that should receive our attention. Who among us would care to be considered a leftist?

The American Board of Ophthalmic Surgeons of the Right Eye will have an august Board of Examiners. For this exacting duty we will turn to the Professors of Ophthalmology. It is only fair, however, that they in turn be rigorously examined before they are authorized to examine candidates for A.B.O.S.R.E. I have devoted much thought to this perplexing question and I have arrived at the following requirements for the Examining Board of A.B.O.S.R.E.:

1. Examiners must be professors of ophthalmology in recognized institutions (a penitentiary is not an institution in this meaning).
2. They must be between five feet and seven feet tall.
3. They must weigh between 100 pounds and 300 pounds. (It is believed that persons over 300 pounds cannot get close enough to the table to acquire sufficient manual dexterity.)
4. Every candidate will be asked to hold the point of a Graefe knife against the tip of his nose. This will automatically eliminate, the palsied, the tremors, and the uncorrected presbyopes.

* These are four of the letters which have been received by THE JOURNAL on surgical certification by the American Board of Ophthalmology. It is not the purpose of THE JOURNAL to prolong the controversy which actually should be taken up before medical societies for discussion and clarification. Therefore, no further communications on either side will be published.

5. All candidates will be escorted to the local tees and given a five iron. Slicers, dribblers, and users of profanity will automatically be eliminated for obvious reasons.
6. No examiner will be accepted who has operated more than four times on the same eye.

It will thus be seen that the requirements for Examiner are so rigid and exacting, that few indeed will achieve that status. The duties of the Examiners will be to meet yearly at the call of the president, to elect officers and transact such business as may properly come before the board. (No proxies allowed.)

All diplomates of the American Board of Ophthalmology will automatically be certificated, as it is presumed such diplomates have had the requisite training and experience; otherwise, there would seem no excuse for the American Board of Ophthalmology examining anything except a preference for drinks.

The diploma of the A.B.O.S.R.E. will be a thing of grandeur. It will be a red eye *couchant* on a field of scar tissue *rampant*. In the lower right hand corner will be a pterydactyl with a ribbon in its mouth. On the ribbon will be inscribed in flowing letters "Semper pronatus."

This work of art will be suitably inscribed on high quality rolled paper so that the holder may daily recall his high office.

(Signed) Edwin S. Wright.
North Hollywood, California.

Editor,

American Journal of Ophthalmology:

I do not expect this to be published but must express my views to the editors of THE JOURNAL regarding the proposed certification in surgery of the American Board of Ophthalmology. I do this with all respect to yourself and the other elders of ophthalmology to whom I owe my education but I do desire to speak my impressions.

The absurdity of a board within a board will serve only to weaken the parent organization. If present surgical requirements are too lenient they should be strengthened. It behooves every physician who aspires to the American Board of Ophthalmology to obtain the necessary surgical experience and training, either formally or under the sponsorship of a senior surgeon.

Those men whose excellence in other than surgical ophthalmology warrants special notice may be issued a special certificate. They are certainly valued members of our profession but do not merit the certificate of a well-qualified all-around ophthalmologist. Are we so specialized that they cannot become capable surgeons?

Those surgeons of outstanding ability among us are well known and have no need of extraordinary certification, and to the casually interested public such a certificate will mean little.

It will mean more to others. It will be putting a means of control of the practice of ocular surgery within the hands of hospital boards of directors, social welfare groups, sponsors of health plans, insurance companies, and the government. They already use the American Board of Ophthalmology for this.

Let us not weaken our board by creation of a superboard. Let us not follow this road of bureaucracy but rather further examine the requirements already present and methods of determining that they are met.

(Signed) Daniel W. Mathias,
Akron, Ohio.

Editor,

American Journal of Ophthalmology:

I wish to express my displeasure in the article written by Dr. Frederick C. Cordes when he chastises those doctors whom he called "six-week wonders" and who set themselves up as "eye, ear, nose and throat specialists." Also it appears to me that he is one of the instigators of the idea that all

board members in ophthalmology should be re-examined to test their qualifications in ophthalmic surgery. Personally I see no reason why the present setup isn't satisfactory because I believe that the selection of candidates by the American Board of Ophthalmology is made on an honorable basis and another subdivision into "surgery" is superfluous.

I know there are quite a number of men who have their boards and who do not do eye surgery, but I know many more board members of other specialties who even do general practice, which is not too common among board members in ophthalmology. All present board members took their examinations in good faith and I do not feel that a hierarchy should belittle the fellow who does little or no eye surgery. Dr. Cordes and his "specialty group" should have thought of this surgical subdivision many years ago and not waited until now to do anything about it when the American Board and the American Academy seem so well organized. I would say leave well enough alone as far as a "Fellowship in Ophthalmic Surgery" is concerned or, at least, give the present members their certificates and take a chance that they won't blind someone. I have that much faith in our men (and ladies) that they know their limitations and will refer a case if they feel they are not qualified to handle it.

As to the "six-week wonders" as Dr. Cordes so aptly puts it, let me say that there are very few of these men who haven't diligently studied hard over the years in clinics, short courses, reading, and so forth, to further their knowledge of ophthalmology. I wonder what the attendance would be like at our county, state, and national meetings if such members were not present to learn something from the board members and lend financial support to such gatherings. I do not think there is a single nonboard member ophthalmologist living (and I am one) who does not have the greatest respect for a board member and all that he represents. But, by the same token, there are many qualified ophthalmologists and ophthalmic surgeons who are not board members and who deserve an occasional bouquet from Fellows like Dr. Cordes. Possibly some M.D.s are nothing but glorified glasses pedlars, but believe me they have ophthalmology at heart and want to do everything to further good public relations and give ophthalmology in general and ophthalmologists in particular the respect they so rightly deserve.

(Signed) Ernest H. Dengler,
Pottstown, Pennsylvania.

Editor,

American Journal of Ophthalmology:

THE JOURNAL (January 1957) published the announcement of the creation of a Certificate of Ophthalmic Surgery. The following are some thoughts concerning this announcement.

The proposal to create a certification in ophthalmic surgery contains several unfavorable aspects:

First, it will lower the prestige of the American Board of Ophthalmology.

Second, it will brand as surgically incompetent all ophthalmologists who fail to possess this certificate.

Third, it will prevent qualified ophthalmologists from practicing anywhere but in the larger cities.

The requirements for certification in ophthalmic surgery will be extremely difficult to obtain in areas of smaller population. There are many diplomates of the board practicing today in areas in which neither the surgical volume nor the necessary certified colleagues are easily available. This, of necessity, may prevent them from obtaining certification, and will indirectly and unjustly brand these men as incompetent ophthalmic surgeons. New diplomates will not be able to practice in smaller communities if they desire certification in ophthalmic surgery. Young men desiring to practice ophthal-

mology in smaller communities, faced with the almost insurmountable task of acquiring the qualifications for certification, while at the same time bearing the label of a "non-certified" ophthalmic surgeon, may well decide that to become a diplomate of the American Board of Ophthalmology is not worth the effort. Areas of small population will be deprived of the competent ophthalmology that could and should be available.

The establishment of a certificate of ophthalmic surgery will decrease the prestige of the American Board of Ophthalmology. It will create the impression that present and future diplomates are incompetent in ophthalmic surgery until they have practiced their specialty for at least three years, performed a large volume of surgery, and then obtained certification. Building a surgical practice and acquiring the volume of surgery necessary for the requirements, under these conditions, is practically impossible in small communities.

It is important to remember that in smaller communities, a physician soon becomes very well known; not only his qualifications but his surgical successes and failures as well. It is also to be remembered that most hospital appointments are based on the possession of board certification. If being a diplomate of the American Board of Ophthalmology is not to mean competency in ophthalmic surgery, it is conceivable that major privileges to do ophthalmic surgery may not be granted; thus further decreasing the opportunity to acquire such certification. It is equally conceivable that, in attempting to acquire, as rapidly as possible, the necessary volume of surgical cases, ill-advised or unnecessary surgery may be encouraged.

It is not, to be sure, the intent of the Certificate of Ophthalmic Surgery to deprive present diplomates of the prestige of the American Board of Ophthalmology, but it will surely accomplish this and a majority of the diplomates will automatically become incompetent surgeons. In announcing the creation of the Certificate of Ophthalmic Surgery, the board is, in fact, stating that the majority of present diplomates are incompetent surgeons, for if the feeling was that only a small minority were incompetent, the concept of surgical certification would not have been proposed.

If there has been improper examination for surgical competency, this should be corrected. However, the manner of correction should be such that diplomates may still build practices in small communities, that diplomates will not suddenly be considered incompetent surgeons, and that the prestige of the American Board of Ophthalmology will not be destroyed.

(Signed) James C. Canniff,
Torrington, Connecticut.

BOOK REVIEWS

THE VISUAL FIELDS: A TEXTBOOK AND ATLAS OF CLINICAL PERIMETRY. By David O. Harrington, M.D. Saint Louis, C. V. Mosby Company, 1956. 314 pages, 234 illustrations, nine color plates, bibliography, index. Price: $16.00.

Dr. Harrington is clinical professor of ophthalmology at the University of California School of Medicine. He is well known for his invention of a "black light" perimeter and for his excellent multiple pattern apparatus which is growing rapidly in use and popularity. He is widely experienced as a neuro-ophthalmologist and teacher in perimetry at the University of California. He was trained by Dr. H. M. Traquair.

This is a splendid book, written with great skill, imagination, and fun. Those of us who saw Dr. Harrington's exhibit at the American Academy of Ophthalmology and Otolaryngology meeting last October were greatly impressed with the clarity and beauty of his charts and diagrams. Well, they are all here for us to study carefully at our leisure.

Perimetry has the reputation of being drudgery and a tiresome thing. It is usually delegated to one's nurse or office worker.

Yet, we all know the enormous clinical value of perimetry and cannot practice efficiently without it. Anything that stimulates us to do better perimetry and get some fun out of it in addition is a great help. Dr. Harrington's book will go a long way toward stimulating our interest.

The book is beautifully printed and illustrated, as already mentioned. It covers the entire field of perimetry, better I think than any book yet published on the subject. It should be in the hands of every neurosurgeon, neurologist, and ophthalmologist.

Derrick Vail.

TRANSACTIONS OF THE PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY, 1956. Volume 37. Edited by Orwyn H. Ellis, M.D. Los Angeles, California, Morrissey Bros., printers, 1956. 369 pages. Price: Not listed.

The Pacific Coast Oto-Ophthalmological Society, now consisting of 660 active members, was launched in 1911 when Ernst Fuchs delivered the Lane Lectures in San Francisco. The annual five-day meeting follows a pattern similar to that of the American Academy of Ophthalmology and Otolaryngology (than which no better model could be chosen) with a superlative scientific program, adorned by a distinguished guest lecturer, motion pictures, and instruction courses. Outstanding in this beautiful volume are the presidential address by Lester T. Jones on epiphora; the differential diagnosis and management of proptosis by Albert C. Furstenberg, guest lecturer; experimental scleral surgery of the monkey by Asbury and Vaughan; differential diagnosis of superficial keratitis by Thygeson and Kimura; vascular lesions of the visual pathways by Alexander; lid injuries by Singer; and pediatric anesthesia by Stringham. As the by-laws of the society permit publication of papers in other journals, several of the contributions have already appeared in THE JOURNAL.

To paraphrase Bishop Berkeley, westward the course of ophthalmology takes its way, as this fine tome amply testifies. It is very much worth reading and having.

James E. Lebensohn.

THE ANATOMY OF THE HEAD AND NECK. By Barry J. Anson, M.D. Philadelphia, W. B. Saunders Company, 1956. 94 pages, 92 plates, index. Price: $6.50.

The author is the professor of anatomy, Northwestern University Medical School, whose many contributions to the field of otology are particularly well known. This work consists of an atlas of gross anatomy, the dissections pictured being serially presented, and is intended to meet the special needs of the doctor in dental practice. However, all physicians whose professional interests lie above the shoulders will find it of value. The line drawings, reproduced for the most part in black and white, are clearly executed, and the parts are adequately and clearly labelled. The drawings of the eye and orbit are standard, although not to scale and obviously are not designed to be of minute interest to the ophthalmologist.

It is a handsome and handy (thin) book bound in a spiral filler cloth cover, thus permitting one to expose the plates on the flat, a most useful device. It represents definitive and meticulous work by an expert.

Derrick Vail.

AN ATLAS ILLUSTRATING THE TOPOGRAPHICAL ANATOMY OF THE HEAD, NECK, AND TRUNK. By the late Johnson Symington. Springfield, Illinois, Charles C Thomas, 1956. Thirty-four plates on cards 19 by 12 inches. Price: $21.00.

The first series of the *Atlas* appeared in September, 1917, and consisted of 25 plates and two reconstructions. A few months later a second series was published with the addition of five plates and two reconstructions. It was very popular for years. In 1954 the

Council of the Anatomical Society of Great Britain and Ireland decided to reprint the *Atlas* without alteration. The plates are on heavy glossy paper and, while I do not know the method of reproduction employed, it looks very much like photographic reproduction. It is well done. The plates are contained in a flat cardboard box with a binding cord and are a tight fit so that it is difficult to replace a chart without risking tearing it. The plates are representative cross sections of the head, neck, and trunk of two cadavers and are meticulously labeled. The relationships are accurate. Those of the head are of great interest and instruction to ophthalmologists and are worthy of careful study.

Derrick Vail.

THE HEAD AND NECK IN ROENTGEN DIAGNOSIS. (Two volumes.) By Eugene P. Pendergrass, J. Parsons Schaeffer, and Philip J. Hodes. Springfield, Illinois, Charles C Thomas, 1956. Price: $37.50.

This monumental work has been greatly extended and new sections have been added to include the many advances in technique and interpretation in roentgenology. With improved format, new and beautifully printed illustrations and explanatory drawings, enlarged texts and additional chapters, the authors and publisher deserve commendation. The chapter on cerebral angiography is altogether new and is richly illustrated with excellent reproductions of films and drawings. A chapter on the eye and orbit has been added and contains much of interest to the ophthalmologist, though it deals mostly with foreign bodies. The lacrimal drainage system has received more attention. This great work will be acclaimed by roentgenologists the world over, for it is the outstanding authority and reference work on the skull in the English language. The ophthalmologist and all those specialists interested in the head will find these volumes indispensable.

Raymond L. Pfeiffer.

SERVICES FOR CHILDREN WITH VISION AND EYE PROBLEMS. New York, American Public Health Association, 1956. Paperbound, 112 pages, selected bibliography.

Of the estimated 68,000 partially seeing children of school age in America, only about 8,000 receive the benefit of special facilities. Some partially seeing children are being educated erroneously as blind children. About half the states make provision for children with impaired sight in their programs for crippled children. Since children do not complain of their ocular difficulties, nursery personnel should observe children for significant evidence. Few communities have programs for vision screening of preschool children, yet most children of four years of age are able to respond to the symbols presented in the Snellen "E" chart.

James E. Lebensohn.

SERVICES FOR CHILDREN WITH HEARING IMPAIRMENT. American Public Health Association, New York, 1956. Paperbound, 124 pages, selected bibliography.

Only about one third of the present school population receives hearing tests. All states make some provision for the education of deaf children. But still a high percentage of children with hearing loss are not receiving the training they need. The majority of children with severe hearing difficulties have damage to the auditory nerve or brain. Histories frequently reveal rubella infection of the mother in the first trimester of pregnancy, birth trauma or severe anoxia at birth, erythroblastosis fetalis, meningitis or severe virus infections in early childhood.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

7

CONJUNCTIVA, CORNEA, SCLERA

Hoffmann, H. **Acute keratoconus in mongolism.** Klin. Monatsbl. f. Augenh. 129:756-762, 1956.

The acute form of keratoconus was observed in a 14-year-old boy and in a 15-year-old girl. A trephine operation at the most bulging point of the cornea was done in both cases. It is possible that both the corneal lesion and the mongolism are of endocrine origin. (58 references)

Frederick C. Blodi.

Hudelo, A. **Keratoconus. Perforating cautery.** Ann. d'ocul. 189:491-495, May, 1956.

The author employed perforating cauterization of the cornea in three advanced cases of keratoconus, with good results. To avoid a central leukoma, the perforation should be below the cornea's center. The resulting cicatricial contraction will produce the desired flattening of the cone, even when its summit is some distance away. (5 references) John C. Locke.

Oppel, Ottomar. **The clinical picture of megalocornea.** Klin. Monatsbl. f. Augenh. 129:737-756, 1956.

According to the literature and to Oppel's own measurements, the normal corneal diameter lies between 10.34 and 12.98 mm. Megalocornea is frequently a hereditary anomaly. It may be recessive and sex-linked and combined with an early cataract. It may be a dominant trait combined with a large lens. It may accompany Marfan's syndrome, gargoylism, craniostenosis, and other abnormalities. It is always combined with some degenerative lesion in the eye or in the body. A large cornea without any accompanying degenerations should be called macrocornea.

A family was observed in which megalocornea occurred as a sex-linked trait. It affected only males, was usually bilateral and was accompanied by a luxated lens, cataract, Krukenberg spindle, embryotoxon or corectopia. The cataract was extracted in one patient. Vitreous was lost and the loop had to be used. A number of provocative tests remained negative in three members of this family. (11 figures, 42 references) Frederick C. Blodi.

Passow, Arnold. **Treatment of corneal infections with a combination of electrocautery, antibiotics and sulfonamides.**

Klin. Monatsbl. f. Augenh. **129**:721-731, 1956.

In the beginning of superficial infections, medical treatment alone is usually sufficient. In cases of frank ulcerations the electrocautery should be used to remove infected and necrotic parts of the cornea. This can be done at the slitlamp. The tip of the cautery is heated up to 100-120°C. Antibiotics or sulfonamides should be used after the cauterization. (7 figures, 18 references)

Frederick C. Blodi.

Purshev, F. **The treatment of phlyctenular diseases of the eye with paraminosalycilic acid.** Vestnik oftal. **6**:41, Nov.-Dec. 1956.

Sixty-four patients with phlyctenules were treated with PAS. In 24 eyes there was superficial and in six deep keratitis. The treatment was topical, by instillation of drops four or five times daily of a 2.8 percent solution of PAS and tablets per mouth.

The majority of the patients were cured within 6 to 12 days. The phlyctenules and corneal infiltrates were absorbed and the visual acuity was restored to normal. During two years of observation recurrences were much rarer than after other methods of treatment. Olga Sichevska.

Quintieri, C. **Unusual concomitant manifestations in ophthalmic herpes zoster and in herpes febrilis of the cornea.** Boll. d'ocul. **35**:56-64, Jan., 1956.

The author describes three cases of rather unusual eye complications in virus infections. In one male patient, herpes zoster of the ophthalmic division of the trigeminal nerve was accompanied by an inflammation of the optic nerve in its intraocular and retrobular portions. There was a resultant marked impairment of the visual acuity. In a second patient, dendritic keratitis of the right eye was complicated by a right central facial paresis. In the third patient, left superficial herpetic keratitis became evident shortly after the appearance of paresis of the left lateral rectus muscle. (3 references)

William C. Caccamise.

Volokonenko, A. **The classification of keratitis according to the pathogenetic principle.** Vestnik oftal. **6**:3-10, Nov.-Dec., 1956.

Volokonenko states that the present numerous classifications of keratitis are based on incorrect grounds. He expresses his opinion that the only sound classification of keratitis should be on the basis of the pathologic changes in the cornea, combined with the etiologic factors whenever possible.

On the basis of many years of study of inflammations of the cornea, the author suggests a classification which, he says, needs further perfection. Some case histories illustrate the author's point.

His conclusions are as follows: 1. In the classification, keratitides are combined according to pathogenetic signs. 2. The role of external and internal influence, also the role of the protective neuro-reflexive mechanism is stressed. 3. The decyphering of the pathogenetic mechanism helps in the planning of therapeutic measures, particularly in those cases in which the etiologic factor is not known.

Olga Sitchevska.

Vozza, R. **A particularly severe case of bilateral necrotizing scleritis.** Boll. d'ocul. **35**:43-55, Jan., 1956.

The author describes a case of bilateral progressive scleroperikeratitis. The course was particularly malignant, and enucleation of both eyes was required. Histologic study revealed a tuberculous etiology. (3 figures, 50 references)

William C. Caccamise.

von Zahn, C. **Didrosulfon in the treatment of keratitis and conjunctivitis.** Klin. Monatsbl. f. Augenh. **129**:833-835, 1956.

Didrosulfon is a combination of Aristamid and dehydrostreptomycin. It is given locally as drops. 50 patients were treated. It proved to be effective against staphylococci, pneumococci, diplobacilli and streptococci. The results in four patients with herpes of the cornea were encouraging. Frederick C. Blodi.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Basile, G. **A case of sympathetic ophthalmia with recovery through penicillin therapy.** Boll. d'ocul. **35**:81-91, Feb., 1956.

The author discusses the case of a 60-year-old woman who refused enucleation for absolute glaucoma. After an iridectomy the eye remained highly irritable; 47 days after the initial procedure the eye was enucleated. By that time the remaining eye had become injected and photophobic and had keratic precipitates. Fundus examination revealed an incipient papilloretinitis. On the basis of these findings a diagnosis of sympathetic ophthalmia was made. The patient was given large doses of penicillin systemically. The eye recovered with a final vision of 8/10. (17 references) William C. Caccamise.

Dolcet-Buxeres, L. **Tuberculosis of the choroid and isoniazid.** Arch. Soc. oftal. hispano-am. **16**:584-591, June, 1956.

The author calls attention to the greater incidence of choroidal tuberculosis in cases of tuberculous meningitis and attributes this to the longer course and lowered mortality of tuberculous meningitis because of treatment with streptomycin and isoniazid. Prior to the development of these drugs tuberculous meningitis was rapidly fatal, and choroidal involvement was less frequently reported. At present tuberculosis of the choroid may be encountered in 40 to 50 percent of cases of tuberculous meningitis. The author reports a case in a patient, ten years old, who had been treated for pulmonary tuberculosis, and six months later developed tuberculous meningitis. A study of the fundus revealed old and fresh tuberculous foci; the fresh foci healed under active isoniazid therapy; retinograms illustrate the favorable effect of the therapy on the appearance of choroidal foci which are small and leave fine choroidal scars. (2 figures, 4 references) Ray K. Daily.

Gareis, Richard. **Clinical and histological studies on the cavernous hemangioma of the choroid.** Klin. Monatsbl. f. Augenh. **129**:782-793, 1956.

Five cases are described. In only one patient, a 13-year-old girl, could the correct diagnosis be made before the eye was enucleated. The clinical diagnosis remains difficult. The other patients were past middle age. Small skin hemangiomas were only seen in the young girl and in a 45-year-old woman. (4 figures, 16 references) Frederick C. Blodi.

Jacobs, L., Naquin, H., Hoover, R. and Woods, A. C. **A comparison of the toxoplasmin skin tests, the Sabin-Feldman dye tests, and the complement fixation tests for toxoplasmosis in various forms of uveitis.** Bull. Johns Hopkins Hosp. **99**:1-15, July, 1956.

The authors studied a large group of cases of uveitis of which 107 were diagnosed as granulomatous uveitis. These were exhaustively investigated for etiology and 37 were ascribed to toxoplasmosis on the basis of three criteria: 1. an ocular picture typical of toxoplasmosis, 2. exclusion of other possible granulomatous infections and 3. a positive toxoplasmin skin test, as well as a positive dye test in 1/64 dilution. (At this level there was an 80 percent correlation between skin and dye tests). In all, 22 cases were treated with Daraprim (25 mg/day for three weeks and then 25 mg. every other day for three weeks) and sulfadiazine (2 gm./day

for six weeks). Thirteen patients showed definite improvement on this regime; however, there were systemic reactions in eight, ranging from leucopenia to agranulocytosis. (10 tables, 13 references)

David Shoch.

Kozakiewicz, Angelina. **Spontaneous free iris cyst.** Klinika Oczna **26**:177-182, 1956.

The author presents a case of a free iris cyst in a woman, 50 years of age. It was brown, had transparent walls and was 2 by 2 mm. in size. It was removed through a simple keratome incision. Microscopic examination showed the presence of connective tissue and cells containing brown pigment which gave a reaction for iron. The author feels that this proves its origin from the posterior layer of the iris. (2 figures, 19 references)

Sylvan Brandon.

Milin, J. and Miletto, G. **Ocular complications of leptospirosis.** Ann. d'ocul. **189**:591-595, June, 1956.

A case of leptospirosis is presented in which a severe bilateral uveitis developed four weeks after the hepatitis and meningitis had subsided. The eye manifestations of the disease are reviewed. (3 references)

John C. Locke.

Milosevic, B. and Blagojevic, M. **Combined therapy of an iridociliary tuberculoma.** Ann. d'ocul. **189**:581-590, June, 1956.

A 22-year-old patient was successfully treated for tuberculous meningitis and miliary tuberculosis with streptomycin, para-aminosalicylic acid, and isoniazid, but developed an iridociliary tuberculoma of the right eye two and one-half months after discharge from hospital. In spite of treatment with isoniazid for 46 days, followed by combined therapy with the three agents for a further 28 days, the condition remained active, the tuberculoma was unaffected, and two new iris tubercles appeared. With the addition of X-ray therapy, however, the tuberculoma commenced to shrink and within three months had entirely disappeared. After an initial increase in exudates, the eye gradually became quiet and the vision returned to normal. The authors ascribe the failure of the chemotherapy to an acquired resistance of the organisms to the drugs during treatment of the meningitis. (1 figure, 18 references)

John C. Locke.

9

GLAUCOMA AND OCULAR TENSION

Couso, G. E., Vasquez, A. and Moücke-berg, F. **The action of diamox in glaucoma.** Arq. brasil. de oftal. **18**:253-274, 1955.

Diamox was administered to nine patients with chronic glaucoma who were hospitalized and given a standard diet. The intake of sodium and potassium was controlled. Tonographic studies, urine analyses and various blood chemistry tests were done. It was found that reduction in ocular tension is not related to the degree of acidosis nor to the decrease of plasma carbon dioxide, both of which result from renal carbonic anhydrase inhibition. The diuretic action of diamox was most pronounced during the first 24 hours of administration, whereas the beneficial action upon the ocular tension persisted throughout the entire period of administration.

Tonography showed that there was no improvement in drainage of aqueous, rather a decrease in production. Studies of the bicarbonate content of the aqueous showed a decrease after the administration of diamox. These results seem to indicate that the ocular effect of diamox is in the ciliary body.

Determination of the sodium and potassium content of the red blood corpuscles revealed a decrease of sodium and in-

crease of potassium, with a relationship between the ocular tension and the change in electrolyte content. It is believed that these cellular changes may also occur in the ciliary epithelium with resultant alterations in the electrolyte content of the aqueous. (13 graphs, 8 references)

James W. Brennan.

Furusawa, T. **The mode of action of some hormones on intraocular pressure.** Acta Soc. Ophth. Japan **60**:1534-1536, Oct., 1956.

An injection of suprarenal extract, anterior pituitary hormone and pituitrin causes a decrease of ocular tension which can be prevented by the addition of tetraethyl ammonium. When the suprarenal gland is removed, a decrease in ocular tension occurs. However, when the pituitary gland is destroyed by diathermy coagulation, an increase in the ocular tension results. From these facts, Furusawa discusses the relationship between the hormone-ocular tension. (11 figures, 4 tables, 40 references)

Yukihiko Mitsui.

Galvez Montes, J. and Moreno Lupianez, E. **Our experience with adrenalin preparations in the treatment of simple, primary and secondary glaucoma.** Arch. Soc. oftal. hispano-am. **16**:573-583, June, 1956.

The mechanism of action of adrenalin preparations on the ocular tension is discussed, and its effect illustrated graphically in six cases of simple glaucoma, three of post-inflammatory glaucoma, four of hypertensive uveitis and three of aphakic glaucoma. The authors found the combination of an adrenalin preparation with a miotic most effective, and effective in cases in which miotics alone failed. The adrenalin preparation is used once daily at first, and then less frequently. One determines by trial the frequency required to hold the ocular tension within normal limits. The authors also found a synergism in the action of diamox and adrenalin preparations; a low dosage of diamox is adequate if given with a simultaneous local application of an adrenalin preparation. (15 tension graphs) Ray K. Daily.

Kolmakova, A. **The evaluation of glaucomatous disease by the dynamic changes of the blind spot.** Vestnik oftal. **6**:20-26, Nov.-Dec., 1956.

The study of the dynamic changes of the borders of the blind spot—the responsive reaction of the perineural zone of the retina to various stimulators—is a valuable aid in the judgment of the progress of the disease and the function of the eye.

The blind spot was examined in the morning hours at 16 points. The examination was done under various conditions: with and without pressure by Baillard's ophthalmodynamometer, by giving bromides or caffein to the patient before the examination, by injecting novocain along the superficial temporal artery, or by causing positive or negative emotions in the patients. The blind spot was examined before and after using these measures.

Of 31 patients investigated, 14 had glaucoma, 2 were glaucoma suspects, 2 had secondary glaucoma and 15 patients had various other eye diseases. Some patients, who received bromides, showed a tendency to a more stable shape of the blind spot, in others, the size of the blind spot showed no stability and it remained enlarged. Some patients, in whom emotional upsets were caused, showed narrowing of the size of the blind spot, but other emotionally unstable patients showed enlargement of the spot.

The author stresses the point that conditioned reflex reactions play a big role in the changes of the size of the blind spot. There is a close relationship between the function of the retina and the condition of the cortex of the brain. The general

condition of the patient, his adaptability to various distressing conditions in his life also greatly change the size of the blind spot. Olga Sichevska.

Vila Coro, A. **Treatment of glaucoma by cyclodiathermy.** Arch. Soc. oftal. hispano-am. **16**:561-572, June, 1956.

The literature on the development of this operation, its technique, mode of action, and indications is thoroughly reviewed. The author's technique of choice is cyclodiathermy of the long posterior ciliary arteries. He states that cyclodiathermy may afford excellent results after other operations have proven futile. A current of 50 to 60 milliamperes should be used, a higher intensity being dangerous and a lower inadequate. The type of electrode or diathermy apparatus is of no importance. The operation acts by producing sclerosis of the ciliary body and reducing its secretory activity. Complications are caused by a faulty regulation of the current and operating too close to the limbus. The principal indications for this operation are advanced glaucoma and glaucoma in eyes with vascular disturbances. Ray K. Daily.

10

CRYSTALLINE LENS

Apollonio, A. **An acrylic lens which is fixed in the anterior chamber.** Boll. d'ocul. **35**:314-318, April, 1956.

The author describes a modification of his triangular acrylic lens which is placed in the anterior chamber. This prosthesis consists of a central portion which functions as a lens and three prongs, two above and one below. These prongs supposedly are inserted into the chamber angle without touching the cornea and thus maintain the prosthesis in a fixed position. The author's lens and the method of insertion are somewhat similar to those of Strampelli as described in the latest English edition of Arruga's text book of ocular surgery. (4 figures, 8 references) William C. Caccamise.

Bisceglia, H. and Mosquera, J. M. **Cataracta syndermatotica.** Arch. oftal. Buenos Aires **31**:229-238, Sept., 1956.

Three well-defined groups of cases of lenticular opacities complicating a skin disorder may be established, according to the nature of the latter and to the eventual coexistence of endocrine disturbances. In Rothmund's syndrome, cataractous changes are seen in association to poikiloderma atrophicans vasculare and to hypogenitalism. In Werner's syndrome, the opacities occur in conjunction with diffuse symmetrical scleroderma; hypogenitalism is also almost constantly present. Andogsky's syndrome consists of a cataract appearing late in the course of an atopic dermatitis (chronic urticaria, prurigo, eczema). In all of them, the condition is often hereditary and of a recessive character.

Less frequently, the lens participates in other, mostly chronic, diseases of the skin, such as psoriasis, rosacea, pemphigus (especially pemphigus foliaceus, where the opacities seem to be a prominent feature of the clinical picture), erythema exudativum multiforme, alopecia universalis and keratosis pilaris. While a shield-like appearance has been ascribed classically to dermatogenous cataract, the opacity then being subcapsular and of an axial location, it must be said that this is by no means an invariable rule.

Six cases are presented; two of them, occurring in monozygotic twins, belonged to the second group described; three corresponded to the third group; in the last case, the lens changes complicated rosacea in a 30-year-old woman. (9 figures, 1 table, 37 references) A. Urrets-Zavalia, Jr.

Buesa, Lorente. **Our suture for cataract extraction.** Arch. Soc. oftal. hispano-am. **16**:602-608, June, 1956.

A limbal conjunctival flap 4 mm. wide is dissected down to the limbus; a double armed suture on Kalt needles is passed through the episclera 1 mm. from limbus at 12 o'clock. After the keratotomy with keratome and scissors and the iridectomy, the two needles are passed through the conjunctiva from within outward at its junction with the limbus; the lens is then extracted, the iris replaced and the suture tied. Two lateral Castroviejo or McLean sutures are then inserted. Five conjunctival sutures close the conjunctival incision. The complications in 151 cases in which the author's suture was used are tabulated. The complete covering of the keratotomy wound by the author's suture is considered insurance against infection and the firmness of the closure permits elimination of an iridectomy, except in restless or coughing patients. (10 figures, 1 table, 34 references) Ray K. Daily.

Caballero del Castillo, Daniel. **Iridectomy and closure of the anterior chamber in cataract extraction.** Arch. Soc. oftal. hispano-am. **16**:597-601, June, 1956.

The author describes a suture for closing the keratotomy wound in cataract extraction, which closes the anterior chamber hermetically and an iridectomy becomes unnecessary except in complicated cases. The closure is made with a corneoconjunctival suture, and three corneocorneal sutures, using for the latter extremely fine silk. The operation begins by anchoring in the cornea four sutures, approximately at 9:30, 11, 1, and 2:30 o'clock. The keratotomy is then made with knife and scissors, and three border-to-border sutures inserted between the previous sutures. After the lens delivery the three border-to-border sutures are tied. The first four sutures are then inserted into the conjunctiva, which brings the conjunctiva down over the wound and covers the incision completely. (4 figures) Ray K. Daily.

Giardini, A. **Absence of the anterior chamber after cataract extraction.** Boll. d'ocul. **35**:275-292, April, 1956.

The author presents a very practical discussion of the unpleasant problem of absence of the anterior chamber following cataract surgery. In order to carry out a systematic examination in such cases it is necessary to resort to various procedures (biomicroscopy with measurement of the depth of the anterior chamber and evaluation of the fluorescein test, ophthalmoscopy, diaphanoscopy, gonioscopy, tonometry, and tonography). After the operation the anterior chamber may assume one of five different appearances in relation to the distance between the cornea and the iris: 1. none, 2. markedly diminished, 3. diminished, 4. aphakic, 5. absent or markedly diminished in a particular sector. It is important to differentiate between a failure to reform and a collapse of an anterior chamber that had reformed. The first condition is present in 3.5 percent of the cases, the second in 5 percent.

Absence of the anterior chamber is not related to the type of incision, but collapse of the anterior chamber is related to the location of the sutures. Absence of the anterior chamber is more frequent after intracapsular extractions, and is rare after extracapsular extraction, particularly if a total iridectomy has been performed. The author has never had a case of absence of the anterior chamber when there was loss of vitreous. Absence of the anterior chamber is always associated with marked hypotonia and a more or less pronounced choroidal detachment.

Absence of the anterior chamber can produce glaucoma which is due to obstructed outflow resulting from the formation of anterior synechiae. Other complications are iritis, opacification of the cornea, epithelization of the anterior chamber, peripapillary or macular edema, opacification of the vitreous, posterior

uveitis, and delayed infection.

The pathogenesis of absence of the anterior chamber following cataract surgery is also discussed. It can result from 1. filtration of the aqueous through the wound, 2. pupillary block and 3. reduction in the secretion of aqueous. According to the author wound leakage is the causative factor in cases of collapse of the anterior chamber, and reduction in the formation of aqueous is the causative factor in failure of formation of the anterior chamber. Methods for prevention and treatment are presented. (46 references)

William C. Caccamise.

Sunde, Olaf Aga. **Senile exfoliation of the anterior lens capsule.** Acta Ophth. Suppl. **45**:1-85, 1956.

The objective of this study was to resolve the conflict in the conception of this process between that maintained by Malling and Busacca, and that of Kraupa and Vogt. The clinical examination of patients with exfoliation of the lens capsule suggests that the essential feature of this process is a deposit of granular material on the surface of the lens; as this deposit is not found on the part of the lens in a surgical coloboma of the iris, it is concluded that proximity or contact between the posterior surface of the iris and the anterior surface of the lens capsule is a necessary condition for the appearance of the deposit on the lens surface. In 32 eyes of 21 glaucoma patients with exfoliation which were examined gonioscopically, the author did not encounter the veiled appearance due to exfoliated material described by Gradle and Sugar; in six cases he found a few flakes in the lower angle of the anterior chamber. Sunde particularly stresses the difference in the appearance of the peripheral band and bridges and of the central disc. He examined with the slitlamp 23 eyes with exfoliation enucleated for glaucoma. In 14 of these exfoliation was diagnosed before enucleation. The data thus obtained show that the granular material forms a deposit found on the posterior surface of the lens, on the back of the iris, on the zonular fibers, and on the hyaloid membrane. Histologic examination of one eye is reported in detail. It supports Busacca's view of the nature of these deposits. In order to determine whether the deposits of Busacca occur only in eyes with exfoliation the author checked the records of 213 enucleated eyes. Deposits of Busacca were found in 26 of these; the record showed that in 22 of these eyes exfoliation was recorded clinically. The other four cases, as indicated by the records, did not permit a thorough clinical examination, because of painful eyes or opaque corneas. The literature on this condition is critically reviewed, and the conclusion is reached that the histologic findings described in Vogt's clinic do not provide sufficient ground for the contention that these findings represent the histologic picture of senile exfoliation of the anterior lens capsule. The author's data support the contention of Malling and Busacca. (37 figures, 106 references)

Ray K. Daily.

Svesdlov, D. **Artificial acrylic lens.** Vestnik oftal. **6**:36-39, Nov.-Dec., 1956.

This is a review of the literature on Ridley's acrylic lens. The lens itself, the technique of the operation, the modifications by Barraquer are described in detail.

Olga Sitchevska.

11

RETINA AND VITREOUS

Berrettini, G. L. and Aulicino, A. **Retrolental fibroplasia.** Arq. brasil de oftal. **18**:238-242, 1955.

A premature infant is described which was in the acute phase of retrolental fibroplasia involving the periphery of the retina of both eyes. In addition, multiple hemangiomas were present. The infant had been placed in an atmosphere of high oxy-

gen concentration after birth. Treatment by means of cortisone administered orally over a period of two weeks resulted in an apparently complete regression of the lesions and the restoration of anatomic and functional integrity of both eyes five months after cessation of treatment.

James W. Brennan.

François, J. and Verriest, G. **Scotopic campimetry in vascular affections of the retina.** Ann. d'ocul. **189**:549-580, June, 1956.

In vascular diseases of the retina more pronounced field defects can generally be demonstrated when the eye is in the dark-adapted state. In hypertensive retinopathy a central scotoma may be found by scotopic campimetry while the photopic visual field is still normal; and the same is true for diabetic and leukemic retinopathies. In branch retinal vein thrombosis, scotopic campimetry brings out defects which are more extensive and of greater localizing value than those found by ordinary campimetry. The finding of a pericecal scotoma or a unilateral enlargement of the normal scotopic central scotoma may be helpful in confirming a diagnostic of prethrombosis of a retinal vein, and similar scotopic defects are found in retinal periphlebitis. In papilledema, the demonstration of a pericecal scotoma with early changes in the normal scotopic central scotoma, helps to differentiate it from pseudopapilledema. In senile exudative macular degeneration and in the retinopathy associated with angioid streaks pronounced scotopic defects can be demonstrated early. In central serous chorioretinopathy a pericentral scotoma and a pericecal scotoma, absent or barely demonstrable by photopic campimetry, can be demonstrated. (21 figures, 47 references)

John C. Locke.

Hardin, R. C., Jackson, R. L., Johnston, T. L. and Kelly, H. G. **Development of diabetic retinopathy: effects of duration and control of diabetes.** Diabetes **5**:397-405, Sept.-Oct., 1956.

The fundus was studied in 140 juvenile diabetics who were under good control. Retinopathy was graded on a scale of 0 to 9, from normal to proliferative retinopathy. A highly significant correlation was found between the degree of control and severity of retinopathy. However, contrary to a previous study, no correlation was found between the duration of diabetes and the severity of retinopathy. This was attributed to the fact that all durations were in excess of 15 years in this study, and that when one has allowed an average of 13 years for the appearance of the retinopathy, the duration is no longer significant. (6 figures, 8 references)

Harry Horwich.

Hummelt, Klaus. **Anticoagulants in the treatment of central vein thrombosis.** Klin. Monatsbl. f. Augenh. **129**:799-805, 1956.

Heparine is given intravenously immediately and the injection is repeated twice at 8-hour intervals. Simultaneously dicumerol administration should be started and the prothrombin time should be kept at 15 to 30 percent of the normal value for three weeks. Among 18 patients with central vein occlusion only two improved during the treatment and one more patient improved later. Among 17 patients with branch occlusion seven improved during the treatment and one later. The prognosis is especially poor in older patients with hypertension. (3 tables, 20 references)

Frederick C. Blodi.

Kapuscinski, Witold, J. **Pulseation of the reflex seen in the eyegrounds with Gullstrand's binocular ophthalmoscope.** Klinika Oczna **26**:103-110, 1956.

By using the binocular ophthalmoscope of Gullstrand the author was able to see pulsation of the reflex on retinal arteries

in most eyes. Necessary conditions were a widely dilated pupil and steady fixation with the other eye. Movement of the arteries could be seen at the rate of pulsation. The author feels that pulsation is physiologic and has no diagnostic value. (4 figures, 14 references)

Sylvan Brandon.

Kapuscinski, W. J. **Studies on the serpentine pulsation of the retinal arterioles and its clinical value. A contribution to the differential diagnosis of edema of the optic nerve head.** Ann. d'ocul. **189**:459-479, May, 1956.

Serpentine pulsation of the retinal arterioles is visible through the Gullstrand binocular ophthalmoscope in all healthy subjects. The author studied it in 88 patients with various retinal and vascular diseases. The pulse was feeble or absent in the following conditions: 1. narrowing or obliteration of the retinal arterioles, especially in retinitis pigmentosa, 2. optic atrophy, even when the caliber of the retinal vessels was unaffected, 3. occlusion of the central retinal artery, and 4. papilledema of intracranial origin. It remained visible in choroiditis and retinal periphlebitis, and in most cases of papillitis and retrobulbar neuritis. Its presence or absence can thus be of value in the differential diagnosis of edema of the optic nerve head. (3 figures, 17 references)

John C. Locke.

Maegwyn-Davies, G. et al. **The adrenal cortex in diabetic retinopathy: urinary 17-hydroxycorticosteroid excretion studies.** Bull. Johns Hopkins Hosp. **99**:16-22, 1956.

The daily excretion of 17-hydroxycorticosteroids in the urine was measured in diabetics with and without retinopathy and in normal controls. The diurnal variations were also measured as was the excretion of 17-hydroxycorticosterone (Compound F) after a standard test dose. No difference was found between the 17-OHCS excretion of normal subjects and diabetics, however, those with retinopathy excreted more 17-OHCS than those without it. No statistical differences were found in the diurnal variations in the three groups. The excretion of Compound F after administration of a test dose was slightly reduced in the diabetic group as a whole as compared to the normal controls. This study, therefore, neither confirms nor contradicts the hypothesis that the adrenal is involved in diabetic retinopathy. (1 figure, 3 tables, 25 references)

David Shoch.

Sgrosso, S. and Alagna, G. **Clinical and pathogenic considerations of floating vitreous bodies (muscae volitantes).** Ann. d'ocul. **189**:480-490, May, 1956.

Abnormal plasma protein values were found in a majority of 20 patients having muscae volitantes, but no other eye disease or significant refractive error. The dysproteinemia was characterized by a mild decrease in total protein, an increase in gamma globulin, a decrease in albumin, and an almost constant reduction in the albumin-globulin ratio. (14 references)

John C. Locke.

Snodgrass, Marjory B. **Anomalous development of retinal vessels.** Brit. J. Ophth. **40**:754-755, Dec., 1956.

A retinal artery crossing an artery or a vein crossing a vein has never been reported. The author describes one case of each. In both cases the nasal vessel crosses over the temporal. Such crossings probably take place near the disc because the developing retinal vessels lie close to each other in this region. (2 figures, 1 reference)

Lawrence L. Garner.

Verdaguer, Juan. **Simple diathermy operation and scleral resection. Their indications in detachment of the retina.** Arq. brasil de oftal. **18**:243-249, 1955.

The author has had 87 percent success with the diathermy operation in treating retinal detachment, and therefore recommends it as the procedure of choice, since scleral resection seems to afford useful vision in only about 35 percent of patients so treated. Useful vision may be defined as acuity which may range between 0.3 and 1. Diathermy is a simple procedure, easily done and less traumatizing to the eye than other procedures. There are instances, however, where scleral resection is indicated. The main indication is vitreous retraction; retinal shortening with the formation of folds is the second principal indication. The classical diathermy procedure is almost certain to fail if used in these cases. The presence of a diffuse vitreous opacity is also considered as indication for scleral resection.

It is believed that vitreous traction exists when the retina fails to return after a period of rest during which bandages were applied to the eyes. Undulation of the retina with ocular movement indicates that there is neither marked hyaloid detachment nor extensive vitreoretinal adhesion. A detachment with a prominent bulla, smooth surface, folds and little or no movement indicates the presence of marked vitreous retraction for which resection is indicated. Detachment in aphakic eyes is also an indication for resection, although some authors report favorable results from diathermy applications. It is estimated that approximately 45 percent of aphakic patients with detachment have massive vitreous retraction. This factor plus the difficulty in localizing retinal holes in aphakia make resection the operation of choice. Resection is also preferable with marked hypotony, multiple holes in different quadrants and in disinsertions from the ora serrata. Study of the retina and vitreous with the slit lamp and Hruby lens is valuable. In some cases with vitreoretinal adhesions, the injection of air or saline solution into the vitreous cavity aids in the reapplication of the retina. James W. Brennan.

12

OPTIC NERVE AND CHIASM

Pinero-Carrion, Antonio. **Retrobulbar optic neuritis caused by digitalis intoxication.** Arch. Soc. oftal. hispano-am. **16**:592-596, June, 1956.

After a brief reference to the literature the author reports a case in a woman 70 years old. After four months of digitalis therapy she noticed a yellow spot in the central field; visual acuity was reduced to 20/40 and there was a bilateral five-degree central scotoma. Interruption of the intake of digitalis led to improvement within two days, and after seven days the scotoma disappeared and vision was normal. (4 references) Ray K. Daily.

Stagni, S. **Variations in the permeability of the blood-aqueous barrier after the retrobulbar injection of nicotinic acid in chronic retrobulbar neuritis and in partial optic nerve atrophy.** Boll. d'ocul. **35**: 330-336, May, 1956.

Using the method of Amsler and Huber (determination of the time required for the appearance of fluorescein in the anterior chamber after its intravenous administration), the author found that the fluorescein appeared more quickly in the aqueous of patients who had been given a retrobulbar injection of nicotinic acid. Ten patients with retrobulbar neuritis and five patients with partial optic nerve atrophy were used in the investigation. (4 figures, 8 references)

William C. Caccamise.

13

NEURO-OPHTHALMOLOGY

Amghi, E. and Saginario, M. **Isolated paralysis of the oculomotor nerve. Clinico-arteriographic considerations.** Riv. oto-

neuro-oftal. **31**:403-424, Sept.-Oct., 1956.

The authors describe the ocular and arteriographic findings in 11 cases of oculomotor paralysis. Such paralysis is usually complete and total. Manifestations of the paralysis initially became evident with ptosis and the picture was completed within a few hours or days. Arteriographic studies revealed a carotid supraclinoid aneurysm in eight of the eleven patients. Of the three patients in whom an aneurysm was not demonstrated, one had ophthalmoplegic migraine, another had a parasellar mass of an undetermined nature, and, in the third the etiology could not be determined. Isolated paralysis of the oculomotor nerve is found in approximately one-third of patients with an intracranial aneurysm. (6 figures, 33 references) William C. Caccamise

Aschan, G., Bergstedt, M., Goldberg, L. and Laurell, L. **Positional nystagmus in man during and after alcohol intoxication.** Quart. J. St. Alcohol **17**:381-405, Sept., 1956.

An objective method of observing and recording nystagmus (nystagmography) was carried out on 17 healthy people. Positional alcohol nystagmus (PAN) was found to consist of a phase I, an intermediate period, and a phase II. The initial blood alcohol level was 0.38 when PAN I appeared, and 0.33 when it disappeared. The intermediate period then lasted about one and one-half hours. Then, PAN II, called the "hangover" phase would begin about five hours after the ingestion of alcohol was commenced and would occur even if all the alcohol had left the blood by that time. Its duration was about six hours. This work is strongly suggestive of a vestibular origin for alcohol positional nystagmus. The medico-legal implications of such exact patterns are discussed. (5 figures, 31 references)
Harry Horwich.

Drew, Arthur L. **A neurological appraisal of familial congenital word-blindness.** Brain **79**:440-460, 1956.

The literature pertinent to congenital dyslexia is very thoroughly reviewed, and a family is presented wherein the father and two sons were word-blind. The neurologic implications of the condition are discussed in great detail, and the author concludes that there is a basic defect in Gestalt recognition which interferes with visual-verbal comprehension. Perhaps delayed development of the parietal lobes is the anatomic subtrate for the phenomenon. There is good evidence that a dominant form of inheritance is responsible for the familial type. (2 figures, 3 tables, 102 references) Harry Horwich.

MacLatchy, R. S. **Herpes ophthalmicus.** Brit. J. Ophth. **40**:762-764, Dec., 1956.

Severe herpes zoster ophthalmicus occurred in three patients who recovered within six or seven days without serious residual defect. Recovery is ascribed to the injection of 100 mg. of vitamin B_{12} with oral administration of antihistaminics. Lawrence L. Garner.

Quintieri, C. **The syndrome of pseudoglaucoma in a patient with intracranial arterial aneurysm.** Boll. d'ocul. **35**:293-301, April, 1956.

The author discusses the case of a 72-year-old woman with a reduction in vision, a hemianopic nasal field defect and a relative central scotoma. Ophthalmoscopic examination revealed a glaucoma-type excavation of the disc with partial optic nerve atrophy. Repeated tonometry revealed no increase in the intraocular pressure. Angiography revealed bilateral aneurysmal dilatation of the carotid arteries. After three years there was no change in the original findings. (3 figures)
William C. Caccamise.

Reynon, M. **The Foster-Kennedy syndrome and the third ventricle.** Ann. d'ocul. **189**:596-599, June, 1956.

The author describes a case of Foster-Kennedy syndrome due to a tumor of the third ventricle. John C. Locke.

Russell, G. F. M. **Pupillary changes in the Holmes-Adie syndrome.** J. Neurol. Neurosurg. & Psychiat. **19**:289-296, Nov., 1956.

The author describes 14 cases of Holmes-Adie pupillary syndrome and emphasizes the variability in the pupillary changes. Irregularity of pupils was a constant finding, and the irregularity was bilateral in about one-half of the cases. In no case was there any evidence of syphilis. In 11 cases the author injected the stellate ganglion on the side of the defective pupil with procaine. There was generally a constriction of the pupil where there was a preserved reaction to convergence. The author therefore concludes that there is no sympathetic overaction in these cases. On the other hand, instillation of parasympathomimetic drugs resulted in a rather marked constriction of the pupils. The author explains this by an analogy to the overaction of sympathectomized structures to adrenalin. He feels that the essential lesion is in the efferent parasympathetic pathway, probably post-ganglionic and the tonic contraction and delayed relaxation is due to the sensitization of the denervated sphincter to acetylcholine liberated by the intact parasympathetic fibers. (3 figures, 2 tables, 28 references) David Shoch.

Spadavecchia, V. **An additional contribution to the understanding of nasociliary neuritis: true (interstitial) neuritis, and degenerative (parenchymatous) neuritis.** Riv. oto-neuro-oftal. **31**:448-478, Sept.-Oct., 1956.

In this third article on nasociliary neuritis, the author discusses its pathogenesis. The author considers the dysfunction of the nerve fibers and the types of nervous elements involved.

William C. Caccamise.

Wiedersheim, O. **Nystagmus and its etiology.** Klin. Monatsbl. f. Augenh. **129**: 805-814, 1956.

The author denies the existence of a nystagmus center. Nystagmus is a central motor disorder in which normal inhibitions are blocked (pendular type) or unphysiologic stimuli are transmitted (jerky type). (6 figures, 3 references)

Frederick C. Blodi.

14

EYEBALL, ORBIT, SINUSES

Linhart, Randolph, W. **Lethal granuloma of the orbit.** Tr. Pennsylvania Acad. Ophth. **9**:121-124, 1956.

This patient developed a marked unilateral exophthalmus, for which, because of the severe pain, an exenteration of the orbit was done. At surgery, the tumor tissue appeared to extend through the right optic foramen. Soon the left eye developed a palpable mass, with a slough of the inner canthus, papilledema, and finally the left eye had to be exenterated. The patient died of exhaustion. Pathologic report was pseudotumor.

Irwin E. Gaynon.

Tosch, Cäcilie. **Charlin's syndrome.** Klin. Monatsbl. f. Augenh. **129**:835-839, 1956.

In this syndrome the nasal, nasociliary and anterior ethmoid nerves are affected. It is a combination of orbital and periorbital neuralgia with inflammatory reactions of the anterior segment of the eye and in the area of the nose. Three such patients are presented. A cocaine-adrenaline spray into the nose is curative. (1 figure, 32 references) Frederick C. Blodi.

15

EYELIDS, LACRIMAL APPARATUS

Balza, Jorge. **Simple operative procedure for lagophthalmos.** Arch. oftal. Buenos Aires **31**:169-174, July, 1956.

While the defective contraction of the orbicularis muscle resulting from facial palsy can hardly be remedied, the accompanying ectropion with all its untoward consequences may be improved considerably by means of the technique suggested by the Friedenwald-Guyton suture for the correction of blepharoptosis. Two small stab incisions are made in the immediate vicinity of the palpebral commissures; a braided white-silk suture (size 2) is passed along the margin of the sagging lower lid, through the superficial layers of the tarsus, and then upward, beneath the skin and the orbicularis fibers of the upper lid, emerging through two additional small wounds located at the nasal and temporal ends of the upper border of the eyebrow. The suture is then carried through the fascial termination of the frontalis muscle, just over the periosteum, and tied in the depths of the upper temporal incision.

Five eyes were operated upon with this method. In three of these the result was very good; in another it proved insufficient, probably because the suture had not been pulled tight enough; in the remaining one, where the suture had to be removed because of some granulomatous conjunctival reaction at the lower cul-de-sac, the procedure was repeated with a satisfactory final result. (11 figures, 8 references) A. Urrets-Zavalia, Jr.

Bloomfield, Sylvan. **Treatment of chalazia with systemic prednisone.** Mt. Sinai Hosp. J., N.Y. **23**:753-760, Nov.-Dec., 1956.

Seventeen chalazia in eleven adults were treated by oral administration of prednisone. There was a definite reduction in size of the chalazia in 16, and surgery became unnecessary in 13. There was one recurrence. (5 references)

Irwin E. Gaynon.

Borrie, Peter. **Eczema of the eyelids.** Brit. J. Ophth. **40**:742-750, Dec., 1956.

During a five-year period, 238 cases of eczema of the eyelid had been referred by ophthalmologists to the dermatological department and classified as 1. dermatitis medicamentosa, 2. contact dermatitis, 3. suspender dermatitis (nickel sensitivity), 4. infective dermatitis, 5. neurodermatitis, 6. constitutional eczema and 7. undiagnosed eczema. Infective dermatitis formed the largest group as well as the most difficult to treat (32 percent). Its etiology is obscure and a tendency to chronicity is not uncommon. Best treatment was found to be the use of neomycin with one of the steroids. The second largest group, dermatitis medicamentosa (29 percent) was benefited by the same therapy. Contact dermatitis formed the third largest group (20 percent). That emotional disturbances and stress can be responsible for this condition is noted in the 14 cases of neurodermatitis in this series. Sixteen cases were undiagnosed and the lesion was probably an allergic contact dermatitis; the allergen was undiscovered. (5 figures and 3 tables, 8 references) Lawrence L. Garner.

Frezzotti, R. **An infrequently described variety of palpebral hemangioblastoma: the hypertrophic angioma of Ziegler.** Boll. d'ocul. **35**:92-111, Feb., 1956.

The author discusses two cases of hemangiomatous lesion, one in the upper lid of a three-months-old girl and the other in the brow of a six-months-old boy. The histologic findings are described. (13 figures, 26 references)

William C. Caccamise.

Herszenderfer, Aleksander. **Remarks on plastic surgery of the lids.** Klinika Oczna **26**:111-116, 1956.

The author discusses general principles of plastic surgery of the lids. His remarks are based on the observation of 162 cases in the Institute of Oncology in Gliwice. Proper excision of scars or tumors is of primary importance. Transplanted skin may be in the form of a pedunculated flap or a free transplant. Proper handling of transplants and suturing is emphasized. The author feels that selection of proper method of operation and precision of its execution assures a good functional and cosmetic result. (7 references)

Sylvan Brandon.

Natchkepia, M. and Chkoniya, E. **A new nonoperative method of treatment of stenosis of the lacrimal canaliculi.** Vestnik oftal. **6**:33-34, Nov.-Dec., 1956.

In five patients with stenosis of the lower canaliculus the canaliculus was dilated and a silk suture 30 cm. long was introduced with a probe from the canaliculus into the middle nasal meatus along the lacrimal nasal canal. The silk suture was left there from two to three weeks. The time of observation was only from four to six weeks. Olga Sichevska.

Ottonello, P. **Retraction of the superior lid in myasthenia.** Riv. oto-neuro-oftal. **31**:391-402, Sept.-Oct., 1956.

The author presents four cases of unilateral lid retraction as an accompaniment of myasthenia. The opinion is expressed that this rather frequent finding in myasthenic patients is on a purely muscular basis and that it is due to a hyperactivity of Mueller's muscle. This smooth muscle like other smooth muscles in the body, is not very sensitive to the factors which bring about myasthenia. (4 figures, 16 references) William C. Caccamise.

Ricci, L. **Malherbe's benign calcific epithelioma of the lid.** Boll. d'ocul. **35**:130-134, Feb., 1956.

This represents the second case of Malherbe's epithelioma that has been reported in the eye literature. The patient was a 16-year-old girl in whom the epithelioma was located on the right upper lid. Histologic examination confirmed the diagnosis. The lesion is considered to be benign and perhaps arises from embryonic inclusions. (3 figures, 5 references)

William C. Caccamise.

Tagamluk, V. **Molluscum contagiosum.** Vestnik oftal. **6**:40-41, Nov.-Dec., 1956.

Two cases of molluscum contagiosum are reported. In a three-year-old child, a firm round growth, 0.8 cm. in diameter was seen on the margin of the left upper lid. There was an indentation at the center, from which caseous matter could be expressed. The cornea was ulcerated and there was a dermatitis of the lid and skin of the cheek. The content of the growth was removed with diathermy coagulation of the wound. In the second patient, a 21-year-old man, a firm growth, 1.5 by 1 cm., on the left upper lid, which was slowly increasing in size during three years, was removed. In both cases typical corpuscles were found. Olga Sitchevska.

Viallefont, H. **The oculo-salivary syndromes.** Montpellier Med. **49**:561-570, June, 1956.

This article is a general review of diseases in which both the tear glands and the salivary glands are involved. Stevens-Johnson syndrome (erythema multiforme bullosum) and Behçet's disease are mentioned briefly, but most of the paper is devoted to three syndromes: those of Heerfordt (uveoparotid fever), Mikulicz and Sjögren. The author feels that the boundaries of these syndromes are indistinct and that they may be different

forms of a basic collagen disease which involves the whole body rather than just the salivary and tear glands.

David Shoch.

Weerekoon, Lloyd M. **Paraphimosis orbicularis.** Brit. J. Ophth. **40**:756-757, Dec., 1956.

Paraphimosis orbicularis is usually confined to the upper lid and results from trauma at birth, being due to spasm of the orbicularis fibers behind the eversion. This condition is to be distinguished from a true congenital ectropion which is usually associated with other congenital defects, involves either upper or lower lid, and is much more persistent. The former is usually of short duration. Two cases are reported. (3 references)

Lawrence L. Garner.

16

TUMORS

Jain, N. S., Sethi, D. V. and Mahajan, K. C. **Rhabdomyosarcoma of the orbit.** Brit. J. Ophth. **40**:758-761, Dec., 1956.

A case of rhabdomyosarcoma of the orbit is described in a boy, 16 years of age. Radiation therapy afforded considerable temporary relief but recurrences were definitely more resistant to radiation and he died 16 months later. (5 figures, 4 references) Lawrence L. Garner

Payrau, P. and Perdriel, G. **Primary osteoid osteoma of the orbit.** Ann. d'ocul. **189**:628-643, July, 1956.

A case of osteoid osteoma involving the roof of the left orbit is presented. This location does not seem to have been previously mentioned in the literature. (6 figures, 48 references) John C. Locke.

17

INJURIES

Osterczy, Hanna. **Statistics of ocular trauma in children under 16 years of age.** Klinika Oczna **26**:171-176, 1956.

Injuries caused 19.5 percent of disturbances among children seen in 1951 and 1952 in the Eye Clinic of Krakow Medical Academy. Boys were involved in 79 percent and girls in 21 percent. The end results are also presented in statistical tables. The author feels that injuries up to the age of six years are mainly due to the lack of supervision. About 70 percent of injuries can be considered preventable. (4 tables) Sylvan Brandon.

Sédan, J. and Rouher, F. **Ocular injuries by aloe barbs.** Ann. d'ocul. **189**:619-627, July, 1956.

The authors report in detail four cases of perforating injury to the eye by aloe barbs and refer to another 13 cases observed by two of their colleagues. They were unable to find any other references in the literature to this specific injury. The cases showed a similar pattern: an initial symptom-free latent period varying from 30 hours to three days, followed by a severe exudative iridocyclitis, which in some cases progressed to phthisis bulbi. They attribute the severe reaction to a toxic rather than an infective factor, since the condition responded well to cortisone but not at all to antibiotics. (7 references)

John C. Locke.

Szwarc, Barbara. **Localization methods in intraocular foreign bodies.** Klinika Oczna **26**:161-163, 1956.

The author discusses the use of X-ray methods for localization of X-ray opaque intraocular foreign bodies. She feels that simple methods have more use than more complicated ones, despite the greater accuracy of the latter. Modification of the Grzedzielski method has been used successfully in the Lublin Clinic in 46 cases. The modification consists mainly in using the scheme of Grzedzielski drawn on a transparent film and superimposed on the X-ray film. (2 figures, 6 references)

Sylvan Brandon.

18

SYSTEMIC DISEASE AND PARASITES

Balza, Jorge F.: **Takayasu's disease (pulseless syndrome).** Arch. oftal. Buenos Aires **31**:261-266, Oct., 1956.

The clinical picture of this morbid entity, which is characterized by an absence of palpable pulsations in the arteries of the upper part of the body and is due to the partial occlusion of the aortic arch and of its main branches, includes several eye signs and symptoms. Cataract formation, changes in the retinal vessels (segmentation of the blood column, hemorrhages, spasms, obliteration and development of anastomoses), iris atrophy, retinal detachment and primary optic atrophy are among the most commonly recorded disturbances. The etiology is not clear; while some cases seem to be of syphilitic origin, others depend upon a non-specific arteritis appearing mainly in females in early adult life. The prognosis is poor.

The case of a 41-year-old man is reported, in which the following ocular findings were noted: hyperemia of the conjunctiva and sclera in the form of a caput medusae, mydriasis and pupillary rigidity, iris atrophy and vascularization, diffuse opacification of the lens, retinal hemorrhages and vascular neoformation. The systolic retinal arterial pressure was only 20 to 30 mm. Hg. Although the radial pulsations were absent, a feeble carotid pulse could be felt; blood pressure readings were 170/80 mm. Hg, as taken in the lower limbs, and a marked enlargement of the aortic arch was detected roentgenologically. Cataract extraction was performed bilaterally with a poor result; ACTH administration brought about only a slight improvement in the patient's general condition. (1 figure, 20 references) A. Urrets-Zavalia, Jr.

Bietti, G. B. **Recent contributions both to the ophthalmological aspects of diabetes and hypoglycemia and to their treatment.** Boll. d'ocul. **35**:241-274, April, 1956.

The author thoroughly reviews the recent developments in the field of both diabetic and hypoglycemic ocular manifestations. This is the Italian translation of a paper which the author presented at a University of Iowa conference. (9 tables, 144 references). William C. Caccamise.

Guinet, P. **A critical study of the ocular manifestations of hyperthyroidism.** Semaine d'hôp. Paris **32**:3487-3496, Nov. 14, 1956.

The author divides the ocular pictures of hyperthyroidism into three groups: 1. retraction of the upper lid, 2. benign exophthalmos and 3. malignant edematous exophthalmos. The characteristic findings in group 1. are an exposed strip of sclera above the limbus and a lid lag (Graefe's sign). There is no true protrusion of the eye. In group 2. true protrusion develops and is accompanied by the exposure of sclera below the limbus and a slight edema of the lower lid. Both these sets of findings may precede the onset of systemic hyperthyroidism and are usually improved with proper antithyroid therapy. The third group is of most concern to the ophthalmologist, since antithyroid therapy may lead to disastrous consequences for the eye. The author feels that this is a disease of the entire autonomic nervous system rather than just of the thyroid gland. He further states that in all probability little of the experimental work on this disease can be applied to the human patient. (3 references)

David Shoch.

Lavier, H., Lagraulet, J. and D'Haussy, R. **Histopathologic study of an eye with chorioretinitis of onchocerciasis.** Bull. Soc. path. exot. **49**:434-438, May-June, 1956.

The authors report their histologic findings in an eye of a patient who had systemic onchocerciasis and had been blind

almost all of his life. Microfilaria were demonstrable in cysts of the skin but not in the eye. The predominant findings in the eye were vascular in nature. There was proliferation of limbal vessels with perivascular lymphocytic proliferation. In the choroid and retina the arterioles were obliterated in many places and a tissue sclerosis had replaced the inflammatory cells.

A secondary optic atrophy was present which the authors believe results from the obliteration of blood supply to the optic nerve fibers. They feel that this is a toxic process caused by toxins released by microfilaria elsewhere in the body. (8 figures) David Shoch.

Lis, E. O. and Ciancia, A. **Comments on an unusual case of myasthenia gravis.** Arch. oftal. Buenos Aires **31**:145-148, May, 1956.

A seven-year-old boy presented a bilateral exophthalmos of sudden onset, plus a certain limitation in the action of all rectus muscles, without ptosis. Only one month and a half later did the other symptoms and signs of myasthenia gravis appear. Prostigmine administration resulted only in a partial amelioration of the clinical picture. (6 references)

A. Urrets-Zavalia, Jr.

Pallares, J. **Ocular manifestations of a case of Takayasu's syndrome.** Arch. Soc. oftal. hispano-am. **16**:550-560, June, 1956.

This syndrome consists of a chronic obliterative, brachiocephalic arteritis, which gradually reduces the blood supply to the upper portion of the body. The thyroidocervical and vertebral arteries escape the process and serve as a source for a collateral circulation in the neck. An obliteration of the radial pulse is associated with an elevated arterial blood pressure in the lower extremities. The author reports in detail a case in a woman, 37 years old. The ocular symptoms which developed in the course of five years were 1. a low retinal arterial pressure, 2. low ocular tension, mydriasis and rigidity of the pupil in the eye with the better visual acuity, and retained pupillary reactions in the poorer seeing eye, 3. peripapillary arteriovenous anastomosis, forming five reddish trunks emerging radially from the papilla, 4. impossibility of differentiation between the arteries and veins in the anastomosed branches or in the temporal vessels, 5. a large preretinal and vitreous hemorrhage in the retinal periphery, 6. marked dilatation of the retinal veins in the better-seeing eye, 7. arteriovenous shunts in the macular region and intertwining vessels on the disc, 8. numerous small reddish foci similar to diabetic aneurysms, and 9. a rapid appearance of the cataract in the better eye, with a positive Tyndall phenomenon, flattening of the anterior chamber, a dilated, displaced, fixed pupil, with ectropion of the uvea, and atrophy of the pigment epithelium of the iris in one area and rubeosis iridis in another. (3 figures, 8 references) Ray K. Daily.

19

CONGENITAL DEFORMITIES, HEREDITY

Gastren, Jorma. **The significance of prematurity on the eye.** Acta Ophth., Suppl. 44, 1955.

The author defines a premature infant as one who weighs less than 2,500 grams at birth. The literature on the etiology, frequency, and mortality of prematures, and on the etiology and symptoms of retrolental fibroplasia is reviewed. The difference in the eyes of the premature and the normal infant is described. The retina of the premature infant is immature, and the retinal blood vessels are the farther away from the ora serrata, the smaller the premature infant is. The material for this comprehensive study comprises 480 infants born before term and selected on

the basis of their birthweight, and 26 infants with retrolental fibroplasia. The control group consisted of 217 normal weight infants. The average age of the children at time of examination was nine years. The group, therefore, consisted of the prematures who survived, and while the percentage data might be different if the weakest prematures could be included in this study, it is pointed out that as thorough an examination as this can not usually be made in children under the age of five years. They were given thorough ocular examinations, including visual acuity, muscle function, color sense, ocular tension and funduscopy. The data show no significant difference in refraction and color sense in the premature and control group. Amblyopia and disturbances in binocular vision were definitely higher in the premature group. The author attributes this to the fact that the brain of the prematures is predisposed to hemorrhage at birth, and to the fragility of the blood vessels. The incidence of the ocular defects increases with the diminution in the birthweight. The retrolental fibroplasia group consisted of 13 boys and 13 girls, all in the cicatricial stage of the disease. Three were definitely and one probably mentally defective. The ocular defects in this group consisted of enophthalmos, microphthalmos, strabismus, nystagmus, glaucoma, abnormalities in the depth of the anterior chamber, atrophy of the iris, posterior synechia and keratoconus. Of the 26 infants 20 had received oxygen therapy. In none of the 475 prematures who had no oxygen therapy were symptoms of retrolental fibroplasia detected. The most severe forms of retrolental fibroplasia were encountered in infants who received blood transfusions. It is believed that nutrition rich in electrolytes and blood transfusions may aggravate an already existing fibroplasia. (13 tables, 204 references)

Ray K. Daily.

Manzitti, Edgardo. **The craniostenoses.** Arch. oftal. Buenos Aires **31**:137-144, May, 1956.

Following Simmons and Peyton's classification of skull deformities, the author lists the main features of oxycephaly, brachycephaly, scaphocephaly, plagiocephaly, Crouzon's craniofacial dysostosis, Apert's acrocraniosyndactylism and hypertelorism, and presents seven assorted observations of his own. Two of these were cases of brachycephaly, one of plagiocephaly, one of hypertelorism and one an instance of Crouzon's malady. While the remaining two patients were also thought to be afflicted by the latter condition, they seem to correspond more closely to that complex abnormality described by Vogt (Vogt, A.: Klin. Monatsbl. f. Augenh. 90:441, 1933) under the name of dyscephalodactylism, where in addition to a cephalic aberration similar to that described by Crouzon, a severe malformation of the hands and feet exists. It is unfortunate that some of the figures referred to in the text are missing. (11 figures)

A. Urrets-Zavalia, Jr.

Ohrt, Vagn. **Ocular albinism with changes typical of carriers.** Brit. J. Ophth. **40**:721-729, Dec., 1956.

Ocular albinism indicates a pigment deficiency confined primarily to the eyes. The ocular symptoms are very much like those seen in generalized albinism. A Danish family consisting of seven generations with 169 members is reported. Of this number 81 individuals were examined, representing four generations. Eight men had ocular albinism and 14 women showed fundus changes characteristic of carriers. The fundus picture of such females is fairly characteristic although variations may occur. The central area is usually normal whereas peripherally one notes a peculiar map-like pattern of grayish-brown, irregular patches of granular pigmentation. These become larger and

more confluent towards the periphery. The choroidal vessels are clearly visible in the intervening zones. Nine of 11 carriers had translucency of the iris, showing that female carriers may exhibit some abortive signs of ocular albinism. While the fundus findings in carriers are always present, the iris findings may not be. (2 figures, 7 references)

Lawrence L. Garner.

Philip, U. and Walton, J. N. **Color blindness and the Duchenne-type muscular dystrophy.** Ann. Human Genet. **21**: 155-158, Nov., 1956.

A family is reported in which some of the males show a sex-linked type of muscular dystrophy and an incomplete red-green blindness. Of ten males, half show both characteristics, four are color-blind only, and one has only the muscular dystrophy. A mathematical study of the linkage is appended. David Shoch.

Waardenburg, P. J. and Van Den Bosch, J. **X-chromosomal ocular albinism in a Dutch family.** Ann. Human Genet. **21**:101-122, Nov., 1956.

The authors discuss ocular albinism in both complete and incomplete forms and report a very large family of Dutch stock in which many of the males show an ocular albinism and associated color-blindedness. In addition the authors describe a diascleral translucency of the iris which can be demonstrated in females who are heterozygous for this trait. A special light is necessary, since too strong a light gives false positives in light-eyed subjects. This is very important, since it enables the ophthalmologist to forecast with some accuracy the fate of the offspring of daughters of transmitter females. David Shoch.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Diez, Magin A. **Trachoma in Argentina.** Arq. brasil. de oftal. **18**:196-230, 1955.

In this long article the author discusses the public health aspects of trachoma in Argentina and the efforts of the government and health agencies in controlling and eradicating it. James W. Brennan.

Pino, Ralph H. **Distribution responsibilities of the specialties represented in the scientific assembly.** A.M.A. Arch. Ophth. **56**:282-287, Aug., 1956.

The author discusses the responsibilities of ophthalmologists in the direction and distribution of eye care.

G. S. Tyner.

Villaseca, A. **Ophthalmology in the United States.** Arch. chil. de oftal. **13**:28-53, Jan.-June, 1956.

The author discusses the residency system, which does not exist in Chile and the work which he saw in his visits to different cities, such as cataract extractions and corneal transplants at Castroviejo's and Paton's clinic in New York, retinal detachment surgery at Schepens clinic, and glaucoma surgery at Chandlers clinic. Walter Mayer.

Zembrzuski, Ludwik. **Medical education of Wiktor Szokalski (1828-1837).** Klinika Oczna **26**:97-102, 1956.

The author describes little known facts about the medical studies of the father of Polish ophthalmology, Wiktor Szokalski. His participation in the insurrection of 1830 to 1831, which interrupted his studies, is described demonstrating his patriotism, love for work and study, and his high ethical standards. (8 references)

Sylvan Brandon.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

Deaths

Dr. Nathan Kent Lazar, Chicago, Illinois, died December 14, 1956, aged 58 years.

Dr. George Bond Ridout, La Crosse, Wisconsin, died November 24, 1956, aged 55 years.

Announcements

Histopathology refresher course

A refresher course in histopathology of the eye will be given at the New York Eye and Ear Infirmary, May 13 through 18, 1957, from 2:00 to 6:00 P.M. each day. This course will be conducted by Dr. Bernard A. Roberts and Dr. S. Lawrence Samuels of the Department of Ophthalmic Pathology, Dr. Brittain F. Payne, director. The fee for the course is $100.00 and the number of students will be limited. For further information write to:

Registrar Mabel R. Stewart
218 Second Avenue
New York 3, New York

Miscellaneous

Walter Reed course

The biennial postgraduate course in ophthalmology was held recently at the Walter Reed Army Hospital, Washington, D.C. Maj. Gen. Leonard D. Heaton gave the address of welcome. Dr. Trygve Gundersen, Boston, discussed "Corneal disease"; Dr. Byron C. Smith, New York, "Preparation of eyes for corneal transplant"; Dr. Ramon Castroviejo, New York, "Corneal transplantation"; Col. Francis W. Pruit, Washington, D.C., "Ocular complications in selected medical diseases."

Dr. Charles E. Iliff, Baltimore, and Dr. Merrill J. Reeh, Portland, Oregon, demonstrated "Reconstructive surgery of the lids and orbit"; Dr. Marshall M. Parks, Washington, D.C., "Vertical muscle motor defects: Diagnosis and treatment"; Dr. Arthur Jampolsky, San Francisco, "Exotropia: Diagnosis and treatment."

College of Surgeons

At the sectional meeting of the American College of Surgeons held in Saint Paul, Minnesota, April 8th, 9th, and 10th, the following ophthalmic program was presented:

Dr. Carl J. Rudolph, South Bend, "Choice of anesthesia in cataract operation"; Dr. Richard C. Horns, Minneapolis, "Dacryocystorhinostomy"; Dr. Robert Lundblad, Minneapolis, "Radioactive isotopes in diagnosis of intraocular malignancies"; Dr. Samuel J. Meyer, Chicago, "Goniotomy"; Dr. Walter H. Fink, Minneapolis, "Surgical indications in strabismus"; Dr. Richard C. Horns, Minneapolis, "Choice of suture material in ocular surgery"; Dr. Walter Lees Hoffman, Minneapolis, "Ocular dermoid."

Guest meeting

At the annual guest meeting of the Kansas City Society of Ophthalmology and Otolaryngology, a panel discussion was held on the "Medical aspects of reading problems." Dr. John McLean, Dr. G. O. Proud, Dr. Paul C. Lavborne, Jr., and Dr. Edwin M. Cole, were openers for ophthalmology, otology, psychiatry, and neurology.

Other papers of ophthalmic interest were: Dr. Larry L. Calkins, "Case presentations"; Dr. Hugh L. Ormsby, Toronto, "Herpes of the eye"; Dr. Lorenz E. Zimmerman, Washington, D.C., "Fungus infections of the cornea and vitreous: A complication of modern therapy"; Dr. David D. Donaldson, "Corneal dystrophy"; Dr. A. N. Lemoine, Jr., "Review of surgical procedures for retinal separation"; Dr. Ormsby, "Interesting ocular conditions"; Dr. Joseph S. Haas, Chicago, "Primary glaucoma"; Dr. Ormsby, "Ocular therapeutics"; Dr. Zimmerman, "Heterochromia iridis and unilateral glaucoma: Signs of diffuse malignant melanoma of the iris"; Dr. Ashley, Dr. McLeod, Dr. Post, and Dr. Shaad, "Symposium on refraction"; Dr. Donaldson, "Corneal degeneration."

Brooklyn program

On the scientific program of the 142nd regular meeting of the Brooklyn Ophthalmological Society, scientific papers were presented by Dr. Willis S. Knighton on "Tonography," and Dr. Seymour Goodstein on "Gonio-photography."

Nassau meeting

The members of the Nassau (County, New York) Ophthalmological Society heard a paper by Dr. Donald M. Shafer on "Vitreous surgery" at a recent meeting.

Personals

Dr. Alberto Urrets-Zavalía, Jr., has been appointed professor of ophthalmology at the Universidad Nacional de Córdoba, Argentina.

Dr. Derrick Vail is honorary chairman of the Board of Directors of the Henry Holland Hospitals Alumni Association and the Henry Holland Mission Hospitals Fund. All alumni of Shikarpur or Khairpur Mirs (give year of attendance) are requested to send a subscription of one dollar or more annually to the alumni treasurer, Dr. Victor E. Lepisto, 210 Quincy Street, Hancock, Michigan.

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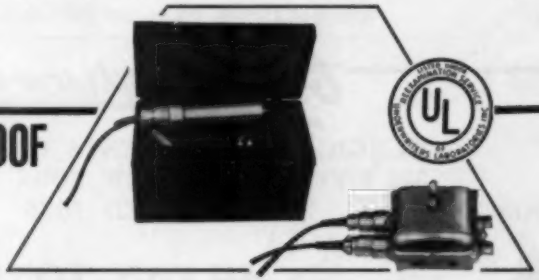

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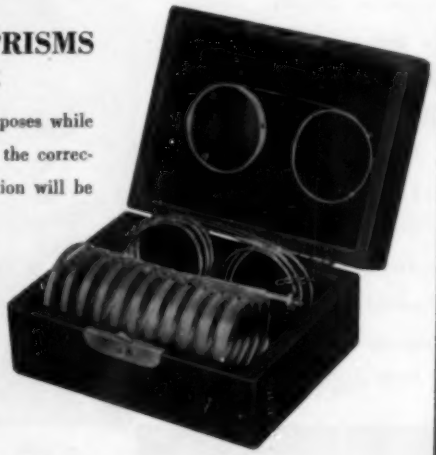

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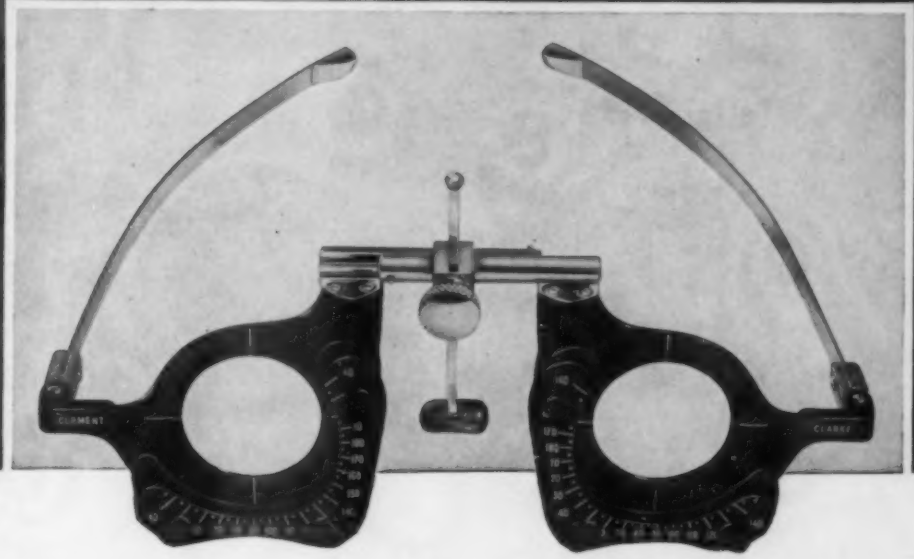

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